13th Post-ECTRIMS Meeting: review of the new developments presented at the 2020 ECTRIMS Congress (I)

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Introduction. For more than a decade, following the ECTRIMS Congress, the Post-ECTRIMS Meeting has been held in Spain, where neurologists with expertise in multiple sclerosis (MS) from all over the country meet to review the most relevant latest developments presented at the ECTRIMS congress (on this occasion held together with ACTRIMS).

Aim. This article, published in two parts, summarises the presentations that took place at the Post-ECTRIMS Meeting, held online on 16 and 17 October 2020.

Development. This first part includes the latest results regarding the impact of the environment and lifestyle on risk of MS and its clinical course, and the role of epigenetics and genetic factors on these processes. Findings from preclinical and clinical research on the lymphocyte subtypes identified and the involvement of lymphoid follicles and meningeal involvement in the disease are discussed. Changes in brain structure are addressed at the microscopic and macroscopic levels, including results from high-resolution imaging techniques. The latest advances on biomarkers for the diagnosis and prognosis of MS, and on the involvement of the microbiome in these patients are also reported. Finally, results from patient registries on the impact of COVID-19 in MS patients are outlined.

Conclusions. There have been new data on MS risk factors, the impact of MS at the cellular and structural level, the role of the microbiome in the disease, biomarkers, and the relationship between COVID-19 and MS.

Key words. ACTRIMS. Congress. ECTRIMS. MS. Multiple sclerosis. Post-ECTRIMS.

Introduction

The 13th edition of the annual Post-ECTRIMS Meeting was held on 16 and 17 October 2020. It was attended by neurologists with expertise in multiple sclerosis (MS) from different Spanish centres who presented the latest developments addressed at the ECTRIMS-ACTRIMS Congress. This is the first of two articles that summarise the Post-ECTRIMS presentations.

Impact of the environment and lifestyle on the risk of MS and its clinical course

Although the aetiology of MS remains unclear, it is known that the disease is the result of an interaction between genetic susceptibility and certain environmental aspects. Along with the risk factors that have already been established [1], there is strong evidence of the influence of exposure to organic solvents, passive smoking, shift work, alcohol and dietary factors on the development of the disease, as well as an effect of smoking on its progression [2].

Obesity and some components of metabolic syndrome are also associated with increased delay in diagnosis, attack rate, brain and retinal atrophy, and disability progression [3-5], with important implications for MS management [6]. Cardiovascular risk factors are already associated with brain atrophy in patients under 50 years of age and have a synergistic effect if present in combination, even when they would be considered mild in isolation [7].

Air pollutants also play an important role in the aetiology of MS. There is an additive interaction between increased ozone exposure and DRB1 alleles in the susceptibility to develop paediatric MS [8]. All these environmental factors appear to interact with human leukocyte antigen (HLA) genes, conferring an increased risk of MS among genetically susceptible individuals.

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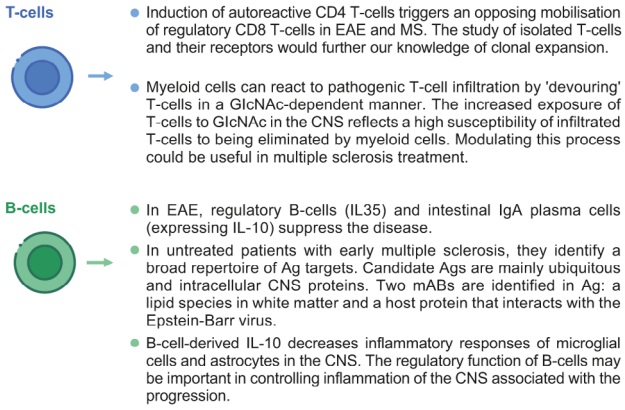
Figure 1. Latest developments related to the study of B and T cells. Ag: antigen; CNS: central nervous system; EAE: experimental autoimmune encephalitis; GlcNAc: N-acetylglucosamine; mAB: monoclonal antibody.



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Epigenetics and genetic factors

The epigenome as a mediator of external variables

One of the modes of epigenetic regulation is DNA methylation. In MS patients, external factors such as disease-modifying treatment (DMT) or body mass index have been shown to affect different cell types by creating cell-specific DNA methylation patterns, and epigenetic variations have been found to be present in axonal signalling pathways [9-11]. Epigenome-wide association studies conducted using deconvolution analysis revealed that epigenetic variations in axonal signalling pathways were present in early stages of MS in specific cells –T-cells, B-cells and natural killer cells (NK)– [12].

A potential drawback of epigenetic studies is confounding bias, as exposure and outcome may have a common cause. To avoid this, it is proposed to use the Mendelian randomisation methodology, which improves causality inferences and could be used when designing clinical trials [13].

Contribution of genetic variants

Genome-wide association studies have identified a total of 233 single nucleotide polymorphisms (SNPs) that increase MS susceptibility. One of these SNPs is rs7923837, located near the *HHEX* gene. In a study of MS patients, the homozygous AA genotype of rs7923837 (rs7923837*AA) was found to determine low levels of messenger RNA expression and increased nuclear translocation of *HHEX*. The higher values in some mitochondrial respiration parameters observed in patients were more pronounced in rs7923837*AA carriers [14].

The polygenic risk score (PRS) is a quantifiable measure to identify groups of people with increased susceptibility to certain diseases. In an analysis of a cohort of 41,505 MS patients and 26,703 controls, and another cohort of 34 families with one parent and at least one child affected, the PRS differed between patients and controls (first cohort) and classified affected siblings in each family with an accuracy of 72% (second cohort). The PRS is an effective measure to identify individuals with a high risk of MS at both the population and intra-family levels [15].

Lymphocyte subgroups

As of the early stages of MS, the central nervous system (CNS) is infiltrated by cells from the adaptive and innate immune system, including mainly $CD8^+$ T-cells and $CD20^+$ lymphocytes, and to a lesser extent $CD4^+$ T-cells. Figure 1 shows conclusions derived from recent findings on T-cell response in MS and in the animal model of experimental autoimmune encephalitis (EAE) [16], potential targets for reducing T-cell pathogenesis [17], B-cell mechanisms of action [18, 19] and the B-cell antigen repertoire in as yet untreated patients [20]. Advances in this field are crucial to understand the pathogenesis of the disease and to develop more effective treatments.

Involvement of lymphoid follicles and meningeal compromise

Meningeal inflammation is one of the key components underlying MS. This inflammation, high in B-cells and compartmentalised within the cerebral sulci, is associated with elevated demyelination and damage to the adjacent subpial cortical grey matter (GM). High meningeal inflammation is associated with increased loss of cortical neurons and microglia activation in the outer layers of the cortex, close to the limit of the cerebrospinal fluid (CSF)/pia mater, compared to the inner layers (surface-in gradient) [21]. It has been hypothesised that meningeal infiltrates could represent one of the main intrathecal sources of inflammatory factors that, released into the CSF, could induce or exacerbate a pathology of the cortex [22]. A study of patients with un-

treated relapsing remitting MS (RRMS) revealed an intrathecal inflammatory pattern that predicted variation in the volume and number of cortical lesions at diagnosis, and distinguished patients at high risk of disease activity after four years with an accuracy higher than 70%. CSF analysis could allow patients to be stratified after diagnosis while also permitting the optimisation of therapeutic management [23].

Neuroimaging studies using 7 Tesla (7T) magnetic resonance (MR) have also shed light on this area. One study showed that there is a correlation between leptomeningeal enhancement (a surrogate marker of meningeal inflammation) and neuronal loss in both the retina –measured with optical coherence tomography (OCT)– and the cerebral cortex (measured with 7T MRI). Patients with leptomeningeal enhancement had greater cortical atrophy and lower retinal thickness. In addition, a diffuse pattern of leptomeningeal enhancement was associated with a faster reduction in the macular and retinal nerve fibre layer [24]. In another study, also using 7T MRI, it was found that patients with leptomeningeal enhancement had increased cortical and thalamic lesions, while those without leptomeningeal enhancement only had increased white matter (WM) lesions [25]. These results suggest an involvement of meningeal inflammation in the development of neuronal atrophy. Its potential use as a surrogate marker in studies evaluating drugs targeting meningeal inflammation is highlighted, together with the usefulness of OCT for measuring such inflammation.

Impact of MS on neurons and glia cells

Neural vulnerability

Neuronal damage and cortical pathology play a key role in the progression of MS. Transcriptomic studies [26] have shown that a selective change in gene expression occurs in certain subtypes of neurons, with excitatory neurons in subpial layers 2-3 sharing the highest level of cortical vulnerability, with an outside-in pattern of progression. These neuron populations also showed increased gene pathways related to cellular stress, protein accumulation, energy metabolism and oxidative stress [27].

Contribution of oligodendrocytes and astrocytes

The role of oligodendrocytes (OLs) in the pathogenesis of MS remains an enigma, but there is evidence that variations in their degree of heterogeneity may contribute to the disease [28]. In EAE, OLs have been shown to express genes involved in MS susceptibility, antigen processing and presentation, immunoprotection, phagocytic capacity and immunomodulatory properties [29-31]. In one study a post-mortem analysis was performed of the WM of four individuals with progressive MS and five controls using single-nucleus RNA-seq (whole transcriptome sequencing). On comparing the transcriptional profiles of OLs in both groups, the authors saw that oligodendrial heterogeneity was altered in MS: while there was a decrease in oligo6 intermediate cells, oligo1 and OL precursor cell (OPC) nuclei, there was an increase in oligo2, oligo3, oligo5 and imOLG [32].

In relation to astrocytes, a genetic risk variant for MS susceptibility, rs7665090^{G}, has been shown to alter astrocyte function, leading to increased lymphocyte infiltration in the CNS [33]. Moreover, positron emission tomography has shown that perilesional adenosine A_{2A} receptor expression in lesions is associated with progression. Furthermore, *in vitro* studies show that adenosine A_{2A} receptor signalling increases oxidative damage in astrocytes [34]. These findings suggest that the intrinsic responses of astrocytes could be therapeutic targets, particularly in the progression phase.

Remyelination mechanisms

In order to elucidate the origin of remyelinating OLs in MS, a *post-mortem* study compared lesions from patients with early MS and patients with progressive MS. The results showed that remyelination was predominantly performed by pre-existing OLs and was most effective immediately after demyelination. Furthermore, breast carcinoma amplified sequence 1 (BCAS1)-positive satellite cells in the cerebral cortex were found to promote remyelination after demyelination [35].

Given the absence of remyelinating therapies, efforts to find therapeutic targets that allow for the development of therapies are particularly important. Two potential targets have been identified: oncostatin M (OSM), a member of the interleukin-6 family, and its mediator tissue inhibitor matrix metalloproteinase 1 (TIMP-1). While remyelination was completely abrogated in mice with inactivation of the OSM receptor (OSMRβ), over-expression of OSM in the chronically demyelinated CNS triggered remyelination. Astrocyte-derived TIMP-1 drove OPC differentiation in mature OLs *in vitro* [36].

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Grey matter pathology

Cortical and WM damage are concomitant pathological processes, but do not appear to be distributed exclusively according to a specific cortical-fascicular pattern. An *in vivo* study of the spatial specificity of the interdependence between intracortical and WM integrity suggests that there is a common, phase-dependent mechanism [37]. With the follow-up of patients using 7T MRI, it has been shown that, in the early stages of the disease, cortical lesions primarily affect the sulci, followed by the convolutions; the rate of cortical lesion formation is higher in secondary progressive MS (SPMS) than in RRMS, and there is no correlation between the accumulation of WM and GM lesions [38].

GM demyelination is a heterogeneous process that results in loss of neurons [26] and synaptic density, as well as changes in the mitochondria. Based on the observation that in subpial lesions there is an alteration between the ratio of miRNAs and the expression of certain genes and metabolic pathways, serum miRNAs that regulate gene expression in cortical lesions could be detected and used as a marker of the prognosis of cortical damage [39]. Although the relationship between subpial demyelination and neuronal loss is unclear, it has been postulated that there is a selective vulnerability of cortical neurons and OLs to this subpial demyelination, and that neuronal loss is independent of demyelination [39].

A study of over 1,000 patients with radiological (15 years) and clinical (19 years) follow-up has shown that atrophy begins in adolescence, before the onset of symptoms, and progresses in a linear manner. Its appearance is independent of the time of onset of MS, diagnosis, gender or subtype. This suggests that assessments of neurodegeneration should be analysed in relation to patient age rather than disease duration. However, the study did not include healthy controls, so the influence of ageing itself on atrophy is unknown [40].

Biomarkers

The development of biomarkers sensitive to MS-associated changes and applicable in clinical practice remains a challenge. Several biomarkers of conversion from clinically isolated syndrome (CIS) to MS and of disability progression have been identified, including genetic, clinical, fluid (CSF and blood) and neuroimaging biomarkers. Table I shows a summary of the most prominent studies on biomarkers that were presented.

Radiological advances

Spinal cord

The spinal cord is frequently affected in MS, causing motor, autonomic and sensory dysfunction. The importance of the spinal cord for the diagnosis of CIS [45] and differential diagnosis of MS [46] has become more firmly established in recent years. Pathological abnormalities in the spinal cord, such as demyelination and neuroaxonal loss, can be observed *in vivo* with MRI. Recent advances include: (i) recommendations for standardised protocols for diagnosis, prognosis and follow-up [47]; (ii) recommendations on the use of spinal atrophy in clinical practice [48]; (iii) the development of registry-based methods to assess spinal atrophy; (iv) quantitative and multimodal MR imaging to measure microstructural damage to the spine; and (v) neuraxis assessment to understand the pathological changes in disability [49]. Figure 2 shows the conclusions of the MAGNIMS-CMSC-NAIMS consensus guideline and recommended protocols for carrying out MR imaging of the spinal cord.

Spinal cord MRI is important for diagnosis in CIS, and for prognosis in radiologically isolated syndrome (RIS), CIS and the early stages of MS. In patients with CIS, gadolinium enhancement (Gd^+) and spinal cord lesions were independently associated with the development of SPMS. In the presence of spinal lesions and together with two or more Gd^+ lesions there was a 45% risk of SPMS at 15 years; whereas in the absence of spinal lesions and Gd^+ lesions the risk of SPMS was only 5% [50]. Spinal cord volume also predicts progression. In another study, each 1% increase in annual loss of spinal volume was associated with a 28% increased risk of progressing in the following year [51].

High resolution image: 7-T

7T MR images have several advantages over 1.5T and 3T, such as superior image clarity, resolution and perception of anatomical details. Increased resolution is crucial in the detection of the sign of the central vein, which is important in the diagnosis and occurs in 80% of patients [52]. The use of 7T MR also allows for a better characterisation of cortical [38] and thalamic lesions [53], which are potential diagnostic and prognostic biomarkers.

Table I. MS biomarker studies presented at ECTRIMS 2020.

	Aim	Methodology	Results	Conclusions
miRNA in serum and MRI [41]	Classify patients according to miRNA profiles and MR phenotypesa (T_2LV and BPF).	Quantification of T_2LV and BPF of 1.5T MR in cross-sectional (*n* = 1088) and longitudinal cohorts at 5 years (*n* = 153). miRNA evaluated in patients with stable MR phenotype for 2 years (*n* = 98).	• MR: 1/3 of patients showed a dissociation between T_2LV and severity of atrophy, disproportionately in type II. Only type IV experienced a worse EDSS. Older age at baseline and lower BPF predicted phenotype conversion at five years • miRNA by phenotype: miR-22-39 and miR-345-50 (pathogenic) over-expressed in types II and IV. miR-365-59 (protective) increased in type I.	MRI MS phenotypes with high atrophy (with or without ongoing inflammation) show high conversion rates, supporting the partial independence of these processes. miRNA is a promising biomarker for its usefulness in immunological characterisation, but requires methodological standardisation
τ protein and β-amyloid in CSF [42]	Assess whether τ and β-amyloid at diagnosis predict early MS disability and if they correlate with radiological markers	Clinical and radiological variables were collected in 109 patients (82 RRMS) at diagnosis and during follow-up. Radiological markers: >9 T_2 WM lesions, and spinal cord lesions	• Patients with higher τ levels at diagnosis developed greater disability as assessed by MSSS and ARMSS • No correlations were found between β-amyloid and markers of early disability • No differences were found in the levels of τ protein or β-amyloid and the clinical forms • There was a (non-significant) trend of higher τ levels and lower β-amyloid levels with higher T_2 WM lesion burden and spinal cord involvement	τ may play a role as a predictive biomarker in identifying early disability. This is the 1st study to report a correlation between τ and MSSS and ARMSS. The exact role of τ and β-amyloid in the pathophysiology of MS is unknown, and hence studies with a longer follow-up, larger sample size and more data analyses are needed
Transcriptomic profiling [43]	Investigate the transcriptional profile of PBMC from patients with RIS vs. CIS vs. controls	PBMC analysis was obtained with the high-throughput RNA-Seq platform in RIS (*n* = 14), CIS (*n* = 26) and controls (*n* = 16)	• Patients with RIS and CIS were characterised by 455 and 125 DEGs, respectively. Among the CIS-associated DEGs, 65 (52%) were common with RIS • The transcriptional profile of RIS was high in genes associated with the inflammatory response and with the activation of the receptor mechanism of the virus and bacteria pattern recognition	RIS and CIS have a similar transcriptomic profile associated with the inflammatory response. The RIS-specific PBMC transcriptome suggests the occurrence of an initial infection that triggers the immune mechanisms of preclinical stages
GFAP, S100B and NfL in serum [44]	Assessing sGFAP, sS100B and sNfL levels as a biomarker of future relapses in NMOSD with aquaporin-4-IgG	47 serum samples were obtained from 18 patients in remission, followed up for up to 10 years. Patients were stratified according to high/low GFAP (141.6 pg/mL), S100B (8.6 pg/mL) and NfL (33.9 pg/mL)	• High levels of GFAP during the remission phase were associated with an increased risk of future relapses and of experiencing them earlier • High levels of S100B and NfL during the remission phase were not associated with an increased risk of future relapses	GFAP could be a prognostic biomarker of relapses in stable NMOSD that could guide the monitoring of treatment response. The absence of NfL as a neural marker in NMOSD reflects differences in pathogenesis with MS

ARMSS: age-related MSSS score; β-amyloid: beta-amyloid; BFP: brain parenchymal fraction; CSF: cerebrospinal fluid; DEGs: differentially expressed genes; EDSS: Expanded Disability Status Scale; GFAP: glial fibrillary acidic protein; miRNA, microRNA; MSSS: MS severity score; NfL: serum neurofilaments light chain; NMOSD: neuromyelitis optica spectrum disorders); PBMC: peripheral blood mononuclear cells; RIS: radiologically isolated syndrome; S100B: serum s100 calcium-binding protein B; T_2LV: T_2-hyperintense lesion volume; WM: white matter. [a] Type I: low T_2LV, low atrophy; type II: high T_2LV, low atrophy; type III: low T_2LV, high atrophy; type IV: high T_2LV, high atrophy.

Meningeal enhancement patterns

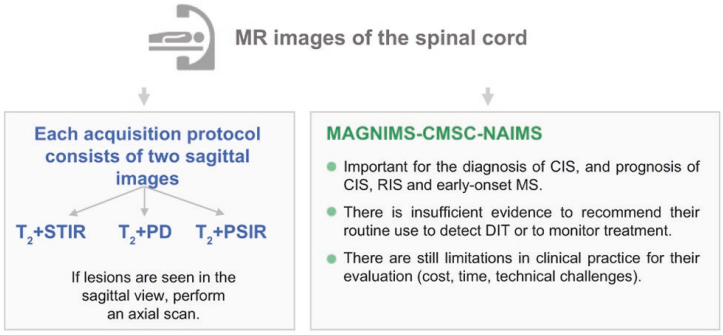
Alongside leptomeningeal enhancement, uptake in the dura mater/falx cerebri and the wall of the meningeal vessels are other, less studied, meningeal enhancement patterns, which are identified with 3D FLAIR (fluid attenuated inversion recovery) MRI and could contribute to the stratification of the MS subgroups. One study has shown that patients with leptomeningeal enhancement have additional vascular wall contrast uptake, compared to those without meningeal enhancement. Dura mater/falx cerebri enhancement is the most frequent meningeal enhancement pattern in MS, and correlates with T_1/T_2 lesion load, with ventricular CSF and with GM brain atrophy [54].

Gut-CNS axis and microbiome

Microbiome compromise

The study of the microbiome is very complex and research in MS patients has been rather limited. Gut bacterial populations appear to be similar in patients and controls in terms of diversity, while the abundance of certain bacteria is not [55]. However, these differences are not always consistent across

Figure 2. Acquisition protocol and recommendations for spinal cord MR imaging. CIS: clinically isolated syndrome; DIT: dissemination in time; MAGNIMS-CMSC-NAIMS: European-based Magnetic Resonance Imaging in MS-Consortium of Multiple Sclerosis Centers-North American Imaging in Multiple Sclerosis Cooperative; PD: proton density; PSIR: phase-sensitive inversion recovery; STIR: short τ inversion recovery.



studies, possibly due to variability in geographic region of origin, diet, comorbidities, medication use and age. Very little is known about the relationship between the microbiome and the risk of relapses, and hardly anything is known about how it is related to disability. Analyses of the main metabolic pathways involved will be essential to identify potential targets for intervention. Some studies show that disruption of up to nine metabolic pathways is associated with risk of relapses and, of these, four involve methane metabolism [56]. Ongoing clinical trials evaluating the effect of probiotic supplements or microbiome transplantation will determine the feasibility of these interventions as disease modifiers [56].

Enteric nervous system

There is currently a debate under way as to whether MS starts in the CNS or whether other peripheral organs, such as the gut, could be considered as a starting point. This possible paradigm shift is supported, for example, by a study showing that 31.6% of MS patients reported gastrointestinal symptoms prior to diagnosis [57].

In a study on EAE, enteric nervous system (ENS) pathology was seen to occur prior to degeneration of the CNS, in the myenteric plexus. The pathology was accompanied by reduced intestinal motility. Furthermore, analysis of colon samples from MS patients revealed nerve fibre degeneration and enterogliosis of the myenteric plexus [58]. Although studies with more MS patients are needed, the role of the ENS in other CNS diseases, such as Parkinson's or Alzheimer's, suggests that there may be a common denominator in neurodegenerative disorders.

Table II outlines the studies presented on the microbiome in paediatric MS [59], the effect of vancomycin on gut permeability in EAE [60], and gut dysbiosis in neuromyelitis optica [61].

COVID-19

Data from a UK registry have shown that the incidence of COVID-19 in MS patients is the same as in the rest of the population [62]. Another registry study, in this case from North America (COViMS), found that when MS patients are classified by ethnicity, African-American COVID-19 patients with MS were younger, more likely to have comorbidities and had a higher risk of worse outcomes compared to Caucasians, even after adjusting for comorbidities in the diagnosis of COVID-19 [63]. The French registry COVISEP identified the Expanded Disability Status Scale and age as independent risk factors for severe COVID-19, while exposure to immunomodulatory DMTs was independently associated with lower severity of COVID-19 [64].

Using the largest international cohort of people with MS and COVID-19 available, an association between anti-CD20 DMTs (ocrelizumab and rituximab) and hospitalisation, ICU admission and use of artificial ventilation was demonstrated, suggesting that their use among MS patients may be a risk factor for more severe COVID-19 disease [65]. Yet, data from the ocrelizumab pharmacovigilance programme showed that mortality in patients treated with this drug (5.5%) can be superimposed on that observed in the general population, and in COVID-19 and MS registries, such as COViMS [66].

Finally, increased humoural immunity in CSF and plasma has been identified in patients with COVID-19 presenting with neurological disorders, although its pathogenic significance is unknown [67].

Conclusions

This latest edition of the Post-ECTRIMS presented advances in our understanding of the mechanisms underlying the onset and development of MS, as well as the role of the epigenome in mediating the

Table II. Studies presented on the microbiome in MS.

	Aim	Methodology	Results	Conclusions
Mirza et al [59]	Examine the functional potential of the gut microbiome by metagenomic analysis of stool samples in paediatric MS	Patients ≤21 years old who met McDonald criteria and with symptoms at onset <18 years old, with no previous treatment or exposed only to IFNB or GA. Illumina NextSeq, Enzyme Comission, MetaCyc and Gene Ontology analyses were used	There was no difference in functional diversity between paediatric MS vs. controls But MS patients showed higher levels of archaeal-related methanogenesis, vitamin B2 production, viral activity, heavy metal metabolism and L-glutamate degradation; and lower levels of homolactic fermentation, and bacterial carbohydrate degradation. DMT affected the relative abundance of tryptophan degradation	Differences in the functional potential of the gut microbiome in paediatric MS vs. controls are observed in several metabolic pathways, including enrichment of tryptophan-related pathways and metabolism of industrial chemicals. Exposure to DMT appears to produce an enrichment of pathways involved in promoting remyelination
Smith et al [60]	Investigate the activity of vancomycin on intestinal permeability in the animal model of EAE	Controls treated with vancomycin and with neomycin. Samples were collected from adult mice before and after inducing EAE in controls and vancomycin-treated mice. Trypsin activity and its role in intestinal permeability were analysed	Vancomycin improved EAE by modulating the gut microbiota, so that vancomycin-treated mice developed milder disease and also preserved the integrity of the intestinal barrier. Proteases, such as trypsin, modulate intestinal barrier function. Vancomycin decreases intestinal trypsin activity and lowers immune activation	Vancomycin preserves the integrity of intestinal permeability through inhibition of intestinal trypsin activity, an effect mediated by the microbiota. Identification of gut bacterial communities that modulate trypsin activity could lead to the development of drugs to prevent and treat MS
Moinfar et al [61]	Study whether an intestinal dysbiosis promotes inflammatory responses in patients with NMOSD	Mice were colonised with stool samples from an untreated NMOSD patient, a household healthy control (HHC) and a vehicle control, and they were examined for susceptibility to EAE induced by MOG p35-55 30 days after immunisation	The mean clinical score of mice colonised with NMOSD gut microbiota was significantly higher than that of mice colonised with HHC gut microbiota or vehicle. The frequency of CD4+ Foxp3+ CD25+ cells decreased in NMOSD and HHC vs. vehicle control, and CD4+Foxp3+Helios+Tregs decreased in NMOSD but not in the HHC group	The data suggest that the intestinal microbiota of NMOSD increases susceptibility to EAE. Decreased Treg contributes to susceptibility to EAE. Several mechanisms may be involved in the worsening of EAE in NMOSD and HHC

DMT: disease-modifying therapy; EAE: experimental autoimmune encephalitis; GA: glatiramer acetate; HHC: household healthy controls; IFNB: interferon beta; MOG: myelin oligodendrocyte glycoprotein; NMOSD: neuromyelitis optica spectrum disorders.

effect of external variables. Despite the discoveries made, the pathological substrate of MS and the relationship between inflammation, demyelination and neurodegeneration remain unknown. As for remyelination, it has been shown that it is more effective when performed by pre-existing OLs than by newly formed OLs. Using 7T MR imaging, it has been shown that there is a correlation between leptomeningeal enhancement and cortical, thalamic and WM neuronal loss, and that atrophy begins in adolescence. The analysis of miRNA, τ protein and transcriptomic profiling stand out as diagnostic and prognostic biomarkers of the disease. Whether there is a specific signature of the microbiota in MS is still unknown, although it is becoming increasingly clear that it is involved in several aspects of the disease.

The incidence and severity of COVID-19 in MS patients is similar to that in the general population. Patients treated with anti-CD20 appear to have a greater risk of more severe COVID-19 and this should be taken into account when initiating or modifying patients' treatment.

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XIII Reunión Post-ECTRIMS: revisión de las novedades presentadas en el Congreso ECTRIMS 2020 (I)

Introducción. Desde hace más de una década, tras el congreso ECTRIMS, se celebra en España la reunión Post-ECTRIMS, donde neurólogos expertos en esclerosis múltiple (EM) de toda España se reúnen para revisar las principales novedades presentadas en el ECTRIMS (en esta ocasión, celebrado junto con el ACTRIMS).

Objetivo. En el presente artículo, publicado en dos partes, se resumen las ponencias que tuvieron lugar en la reunión Post-ECTRIMS, celebrada los días 16 y 17 de octubre de 2020 de forma virtual.

Desarrollo. En esta primera parte se incluyen los últimos resultados acerca del impacto del ambiente y el estilo de vida sobre el riesgo de EM y su curso clínico, y el papel de la epigenética y los factores genéticos sobre estos procesos. Se discuten los hallazgos en investigación preclínica y clínica sobre los subtipos de linfocitos identificados, y la implicación de los folículos linfoides y la afectación meníngea en la enfermedad. Los cambios en la estructura cerebral se abordan a nivel microscópico y macroscópico, incluyendo resultados de técnicas de imagen de alta resolución. También se presentan los últimos avances sobre biomarcadores para el diagnóstico y el pronóstico de la EM, y sobre la afectación del microbioma en estos pacientes. Por último, se esbozan los resultados de registros de pacientes sobre el impacto de la COVID-19 en los pacientes con EM.

Conclusiones. Ha habido nuevos datos sobre factores de riesgo de la EM, impacto de la EM a nivel celular y estructural, papel del microbioma en la enfermedad, biomarcadores y la relación entre COVID-19 y EM.

Palabras clave. ACTRIMS. Congreso. ECTRIMS. EM. Esclerosis múltiple. Post-ECTRIMS.