Trials of vitamin D supplementation have to date lacked de
ulatory independent of Vitamin D, and can regulate CIS to MS
devise for MS brain lesions. Only one out of the four cases had prior infection, and the patients tended to relapse without induction of maintenance therapy.

Conclusion: Our findings indicate that anti-MOG antibody positive brain lesions are highly inflammatory in character, often presenting with meningitis. It is encephalitis with pathophysiology different from anti-AQP4 antibody mediated-astrocytic dysfunction found in seropositive NMO and yet clinically distinct from monophasic ADEM.

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1236
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SHIFT 3 - MS & DEMYELINATING DISEASES
Narrowband UVB phototherapy for clinically isolated syndrome: Delivering the benefits of all UVB-induced molecules
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Background: Trials of vitamin D supplementation have to date lacked definitive outcomes in MS patients. Narrowband UVB can induce vitamin D production, but also other important immune-regulatory molecules in skin.

Objective: The PhoCIS trial (Phototherapy for Clinically Isolated Syndrome) was established in Perth, Australia (32 degrees S), to investigate the clinical, radiological and immunological effects of narrowband UVB phototherapy on MS development in CIS.

Patients and Methods/Material and Methods: Eighteen individuals with CIS have been recruited with 44% of them given narrowband UVB phototherapy of 3 sessions per week for 8 weeks. All 18 participants were supplemented when necessary with vitamin D to 25(OH)-vitamin D levels of approximately 80 nmol/L. MRI was performed after 3, 6 and 12 months, and extensive blood cell phenotyping at 1 week, 1, 2, 3, 6 and 12 months after recruitment. No participant was taking any disease modifying drugs at recruitment.

Results: After 6 months, 7 of 9 participants (78%) without phototherapy converted to MS (McDonald criteria). Only 3 of 8 participants (37.5%) who received phototherapy converted to MS (P=0.09). UVB therapy prevented the increase in memory B cells in the blood of non-phototherapy CIS participants, and produced a significant increase in immunoregulatory IgG4.

Conclusion: These interim results demonstrate UVB effects slowing the progression of individuals with CIS to MS. The PhoCIS trial provides a fresh approach to re-defining the reported associations of 25(OH)-vitamin D levels with MS development and progression. The outcomes suggest that UVB-irradiation of skin is immunomodulatory independent of Vitamin D, and can regulate CIS to MS progression.

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1237
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SHIFT 3 - MS & DEMYELINATING DISEASES
Cytokine activation in cerebrospinal fluid of patients with multiple sclerosis
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Background: Inflammation and leukocyte infiltration of the brain are the hallmarks of multiple sclerosis (MS). Cytokines regulate leukocyte migration across the blood brain barrier (BBB) and play central role in inflammation. Despite the advances in understanding of MS pathogenesis, little is known about cytokine activation in cerebrospinal fluid (CSF).

Objective: To investigate cytokine activation in CSF of patients with MS.

Patients and Methods/Material and Methods: CSF was collected from 20 patients with MS (McDonald 2010) and 20 individuals without CNS inflammatory diseases. Forty eight cytokines were analyzed in CSF using 27-plex and 21-plex Bio-Plex (Bio-Rad, Hercules, CA, USA) multiplex magnetic bead-based antibody detection kits.

Results: Many cytokines, including IFN-γ, chemokine (C-C motif) ligand 5 (CCL5), macrophage migration inhibitory factor (MIF), chemokine (C-X-C motif) ligand 10 (CXCL10), TNF-related apoptosis-inducing ligand (TRAIL), CXCL11, interleukin-2 receptor (IL2Ra), CXCL1, stem cell factor (SCF), CXCL10, were found upregulated in CSF. Also, STRING interaction analysis revealed a connection between IFN-γ and CCL5 as well as MIF. These data suggest the role of lymphocytes and astrocytes in MS brain pathology, since IFN-γ is produced by Th1 lymphocytes, while CCL5 and MIF are released by astrocytes. It has been shown that IFN-γ stimulates astrocyte to secrete CCL5 and MIF. Therefore, we suggest that IFN-γ secreted by activated leukocytes could trigger CCL5 and MIF production by astrocytes. These cytokines can establish the inflammatory milieu and interact with chemokines including CCL27 and CXCL1.

Conclusion: Our data presents activation of multiple cytokines in MS CSF. Our data supports the role of Th1 lymphocytes in the pathogenesis of MS brain inflammation.

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1238
WCN17-1994
SHIFT 3 - MS & DEMYELINATING DISEASES
Efficacy and safety of interferon beta-1a for intramuscular injections biosimilar in patients with relapsing remitting multiple sclerosis
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Background: Interferons beta (IFN-beta) are still among the most frequently used agents for disease modifying therapy (DMT) of multiple sclerosis (MS). Many biosimilars of IFN-beta have appeared recently, but data about their efficacy and safety are controversial.

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Objective: To evaluate the efficacy and safety of IFN-beta-1a for intramuscular injections (IM IFN-beta-1a) biosimilar in Russian patients with relapsing remitting MS (RR MS).

Patients and Methods/Material and Methods: 92 treatment naïve patients with newly diagnosed RR MS (McDonald 2010) were included in study. In all these patients treatment with IM IFN-beta-1a biosimilar (CinnoVex®, CinnaGen Co, Iran) and original IM IFN-beta1a (Avonex®, Biogen, USA).

An effective alternative to the 2nd line disease modifying agents for stabilizing and controlling relapses in aggressive MS in resource limited settings. A longer follow up on a larger cohort is required to confirm these findings.

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1240
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SHIFT 3 - MS & Demyelinating Diseases

Mitoxantrone in aggressive relapsing multiple sclerosis in resource limited settings

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Background: Aggressive relapsing Multiple Sclerosis (MS) is usually managed with IV Natalizumab or oral Fingolimod. However their prohibitive cost prevents usage in resource limited settings. We assessed the efficacy of IV Mitoxantrone in aggressive MS in North Indian patients.

Objective: To determine efficacy of IV Mitoxantrone with pulsed methylprednisolone in aggressive MS in North Indian patients.

Patients and Methods/Material and Methods: 10 patients with aggressive MS were enrolled from the MS registry of our center. They were treated with monthly pulses of IV Mitoxantrone (12 mg/m2) and 1 gram IV methylprednisolone for 6 months and followed up for at least 6 months. Patients underwent monthly echocardiogram and hemogram and liver function tests. The primary outcome was relapse rate and proportion of patients achieving >1 point improvement in Expanded Disability Status Score (EDSS).

Results: The male:female ratio was 3:2, the median age being 37 years. Median disease duration was 5 years. Median follow up period was 12 months. 9(90%) patients became relapse free, 2 (20%) patients worsened with increase in EDSS, 5 (50%) had stabilization of disease with no change in EDSS, 2 (20%) had improvement in EDSS of >1 point. 1 patient had a clinical relapse during follow up. Ambulation was maintained or improved in 70% patients. No adverse effects were reported during the study.

Conclusion: IV Mitoxantrone with pulsed IV methylprednisolone is an effective alternative to the 2nd line disease modifying agents for aggressive relapsing MS in resource limited settings. A longer follow up on a larger cohort is required to confirm these findings.

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Exosomes in intercellular communications by delivering a variety of molecules such as miRNAs, though the pathogenic function of exosomes has not been studied in multiple sclerosis (MS). It has been indicated that regulatory T (Treg) cells are reduced in MS, of which underlying mechanism is still unknown.

Objective: To identify the pathogenic role of exosomes in MS.

Patients and Methods/Material and Methods: Exosomes were collected from the plasma of MS patients or healthy controls (MS-exo, HC-exo). Microarray analysis, RT-qPCR, and culture experiments with exosomes or after transfection of miRNA-mimics/miRNA-inhibitors/si-RNAs were performed.

Results: MS-exo decreased a relative frequency of Treg cells compared with HC-exo in vitro. We performed comprehensive analysis of exosomal miRNAs in MS, for the first time to our knowledge. There was clear difference of miRNA profile between MS-exo and HC-exo. Among them, abundance of let-7i in exosomes correlated with their capability to decrease Treg cells, and inhibition of let-7i restored the decreased frequency of Treg cells. Further experiments suggested that let-7i reduced Treg cells via suppression of insulin-like growth factor-1 receptor (IGF1R) and transforming growth factor-beta receptor-1 (TGFBR1). These receptors were shown to be involved in the differentiation of Treg cells. Furthermore, there was reduced expression of these receptors on naive CD4+ T cells in the peripheral blood of MS patients, and the frequency of Treg cells positively correlated with TGFBR1 expression on naive CD4+ T cells.

Conclusion: This study suggests that exosomes play a pathological role in MS by suppressing Treg cells via let-7i-IGF1R/TGFBR1 axis.

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