study will assess the frequency and severity of ISRs associated with these treatments in patients with relapsing-remitting MS.

BRIGHT is a multicentre, international, non-randomised, prospective study with two treatment arms: 250 mcg IFNB-1b sc eod and 44 mcg IFNB-1a sc tiw. Patients entering BRIGHT must have started treatment within 3 months prior to recruitment, and completed the titration phase. Use of an autoinjector is recommended, but manual injection is also acceptable. Injections will be administered by the patient, and the self-assessed severity of pain recorded for 15 consecutive injections using a 0–100 mm visual analogue scale diary immediately after injection, and 30 and 60 minutes post-injection. Patients will also rate the quality of pain after the 1st, 7th and 15th injections using the McGill pain questionnaire. The occurrence and severity of ISRs will be determined using a 4-point categorical scale. Interim data will be presented.

The BRIGHT study will determine the influence of ISP on patient satisfaction with therapy and highlight any differences in ISRs and severity of pain between the two high-dose, high-frequency IFNB treatments in a routine clinical setting.

P353
Prolactin and multiple sclerosis
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Introduction: Prolactin is a mammotropic neuropeptide produced by the pituitary and extrapituitary cells and has potent immunomodulating properties.

Aim: To investigate the possible correlation of prolactin with MS forms and activity.

Patients-Methods: 33 females (mean age 34) and 7 males with MS (mean age 34) were studied.

Males: mean EDSS: 3.6, Relapsing-Remitting: 4, and Secondary-Progressive: 3.

Females: mean EDSS: 3.2, Relapsing-Remitting: 20 and Secondary-Progressive: 13.

We divided female patients in two groups:

Group 1: Relapse, n = 13

Group 2: Remission, n = 20

Prl was measured in serum using immunoradiometric assay (IRMA) before steroid administration in the relapsed patients.

Results: Prl levels in females range from 93–1104 mIU/l (normal levels = 64–395 mIU/l) compared to males from 144–503 mIU/l (normal range = 78–380 mIU/l). Two men had PRL levels higher than normal. In females the results in the two groups were: Group 1: mean Prl level = 401.69 mIU/l and Group 2 = 368.5 mIU/l.

We did not find any correlation between Prl levels and disease type, EDSS, duration disease, and patient age. Thirteen of the females had Prl levels higher than normal. Three of them, with PRL levels ranging from 1026–1104 had severe episodes of bilateral optic neuritis.

Conclusions: The high levels of Prl in women on exacerbation may suggest its effect in the disease activity. Whether this effect is primary or secondary, cannot be easily confirmed. Prl, a hormone of the hypothalamopituitary axis with immunomodulatory properties, could affect the disease characteristics. In patients with visual disturbances, their symptoms may be connected with lesions close to hypothalamus.

Poster session 3

Cerebrovascular disorders

P354
Assessment of endothelial dysfunction in acute stroke patients: a clinical and laboratory study
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The endothelium plays an integral part in the atherosclerotic process and the occurrence of thrombotic and ischaemic events in the vascular system. vWF (von Willebrand Factor) and t-PA (tissue plasminogen activator) are haemostatic markers reflecting endothelial function.

Objective: The present study was designed to assess endothelial function in acute ischaemic stroke patients by estimating the levels of certain haemostatic markers in serum, and to investigate the possible relationship of these markers to demographic, clinical and imaging data.

Subjects and Methods: 50 patients with acute ischaemic stroke and 27 matched controls were included in this study. All participants were subjected to careful clinical evaluation, laboratory work-up and neuroimaging of the brain.

Results: Mean vWF level was significantly higher and mean t-PA level was significantly lower in stroke patients compared to controls (p = 0.02, 0.001 respectively). Significantly higher vWF levels and lower t-PA levels were also detected among smokers and diabetics of the patient group as compared to those of the control group. Significant increase in vWF and decrease in t-PA levels were observed as the number of risk factors for atherosclerosis increases in the patient group (p = 0.03, 0.002 respectively). No significant correlation was found between vWF and t-PA levels and prognosis of stroke. Levels of vWF and t-PA differed significantly between stroke patients and controls regardless of the presence or absence of risk factors, which indicates that vWF and t-PA can be considered as independent risk factors for cerebrovascular ischemic events.

In conclusion: vWF and t-PA are useful haemostatic markers reflecting endothelial function in ischemic stroke patients and predicting occurrence of future thrombotic events.

P355
Carotid duplex studies in young strokes with a prothrombotic state
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Prothrombotic states like protein C deficiency, protein S deficiency, antithrombin deficiency, the antiphospholipid antibody syndrome, factor V Leiden and hyperhomocysteinemia has been implicated in the etiology of young strokes. These, however, are responsible only for a minor population (~4–6 %). The occurrence of carotid lesions in young strokes is of low prevalence.

Aims and Objectives: To prospectively determine the incidence of carotid/vertebral artery disease in patients of young stroke with a prothrombotic state.

Methods: Patients were recruited from the young strokes attending the Neurology outpatient at PGIMER, Chandigarh who were found to be positive for one or more prothrombotic states viz. Protein C, Protein S or Antithrombin deficiency, Antiphospholipid antibody syndrome, Lupus anticoagulant positive, Factor V Leiden positive or hyperhomocysteinemia. Carotid duplex studies were carried out on these patients which included B-mode, color and pulsed doppler studies.

Results: 186 young stroke patients have been enrolled till December 2004. 63 (33.8 %) patients have been found to be positive for either one or more of the prothrombotic states. 13 patients (20.63 %) have some abnormality in the carotid duplex studies. 6 patients (46.15 %) had Protein S deficiency only, 1 (7.69 %) patient had Protein C deficiency only, 2 (15.38 %) patients were deficient in both Protein C and Protein S, 3 (23 %) patients were positive for Lupus anticoagulant whereas 1 patient was positive for both Lupus anticoagulant and Anticardiolipin antibodies.

Conclusions: 1. Carotid atherosclerosis is an important contributor to strokes of prothrombotic origin. 2.Protein S Deficiency appears to be the most common abnormality to be associated with abnormal carotid duplex findings. 3.These findings could help in formulating an effective screening strategy to search for prothrombotic states in young strokes.

P356
Dissection of the vertebral artery presenting with C5 radiculopathy
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Background: Flaccid paresis of C5 innervated muscles may be due to idiopathic brachial plexopathy or to compression of the C5 nerve root by spondylopathy or discopathy. We describe a case of vertebral artery dissection (VAD) causing C5 radiculopathy and give a review of the literature.

Case report: A 52-year-old male was referred for evaluation of proximal weakness of the left arm. Ten days before he fell onto his right side getting some bruises at the lateral chest. Thereafter he developed some pain in the neck on the left side, responding to Ibuprofen. Three days later he could neither elevate nor rotate the left shoulder. He had no pain and no sensory deficit was noted. Preceding infection was denied. The patient received vaccination for polio and hepatitis three months before.

On admission he presented with severe weakness of m. deltoideus (M2), m. suprascapularis (M2), m. infraspinatus (M2) and m. biceps

creased cortisol serum levels at all five time points as compared to MS patients in remission. TNFR-1 as well as TNFR-2 levels followed a less marked ($p < 0.05$) descending course over the day in all groups. MS patients with Gd-enhancement had again significantly ($p < 0.05$) elevated levels for TNFR-1 but not for TNR-2 as compared to healthy donors. In contrast, IL-4-R and TNF-beta serum concentrations were relatively stable over the day. Both MS groups had significantly ($p < 0.05$) elevated TNF-beta serum levels at any time point as compared with the control group. Moreover, the TNF-beta serum levels were further ($p < 0.05$) increased in the group with active MS patients as compared to patients in remission.

Conclusion: Our data show that the diurnal rhythmicity of immunological markers must be considered in at least some of the investigated immunological markers. We could not observe a substantial difference in the circadian rhythmicity between MS patients and healthy donors. However, the increase of cortisol serum levels in MS patients with active disease shows that MS disease activity has an at least indirect influence on the circadian rhythmicity.

P573

Glatiramer acetate induces pro-apoptotic mechanisms involving Bcl-2, Bax and Cyt-c in peripheral lymphocytes from multiple sclerosis patients

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Apoptotic deletion of autoreactive T-cells is defective in patients with Multiple Sclerosis (MS). Glatiramer Acetate (GA) treatment seems to restore apoptosis of detrimental T-cells. We analyzed the mitochondria membrane pro- (Bax) and anti-apoptotic (Bcl-2) and cytosolic pro-apoptotic (Cyt-c, APAF-1) proteins expression in peripheral lymphocytes from RR MS patients during GA treatment. Blood samples from 8 RR MS patients, before and every three months during 9 months of GA treatment, and from 8 healthy controls (HCs) were collected. PBMNC Bcl-2, Bax, Cyt-c and APAF-1 were quantified by western blot followed by densitometric scanning and Bax/Bcl-2, cytosolic Cyt-c/Bcl-2 and APAF-1/Bcl-2 ratios were calculated. The percentage of apoptotic cells was assessed by a dye exclusion test. T-cells were in vitro tested for oxygen consumption by a respirometric analysis. Bax/Bcl-2, cytosolic Cyt-c/Bcl-2 and APAF-1/Bcl-2 ratios in untreated MS patients were significantly ($p < 0.05$) lower than in HCs. Bax/Bcl-2 ratio increased ($p = 0.03$) and Cyt-c/Bcl-2 ratio showed a trend to increase during 9 months of GA treatment in MS patients. An increase of 85 % in the rate of apoptotic PBMNCs was observed during treatment. A reduction by 58 % in oxygen consumption by T-cells was evident after GA treatment in vitro. Our findings suggest that GA exerts a regulatory effect on peripheral T lymphocytes through pro-apoptosis mechanisms involving mitochondria and cytosolic proteins.

P574

A randomised, placebo-controlled phase II trial of a novel oral single-agent fumarate therapy, BG00012, in patients with relapsing-remitting multiple sclerosis

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Objective: To determine the efficacy and safety of a novel single-agent oral fumarate therapy, BG00012, in patients with relapsing-remitting multiple sclerosis (RRMS).

Background: An open-label pilot study demonstrated that a product containing a mixture of fumaric acid esters significantly reduced the number and volume of gadolinium-enhancing (Gd+) lesions in patients with RRMS. BG00012 is being investigated for the treatment of psoriasis and other autoimmune diseases, including MS. This phase II study was designed to evaluate the efficacy of three doses of BG00012 on brain lesion activity as measured by magnetic resonance imaging (MRI) in patients with RRMS.

Design: This is a randomized, double-blind, placebo-controlled, phase II study being conducted at 45 clinical centers in Europe. Patients were included in the study if they were between 18 and 55 years of age, had a definite diagnosis of RRMS, and an Expanded Disability Status Scale (EDSS) score between 0.0 and 5.0. In addition, patients must have either experienced at least 1 relapse within 12 months prior to randomization with lesions on cranial MRI consistent with MS, or had Gd+ lesions on a cranial MRI performed within 6 weeks of randomization. Eligible patients were randomized to receive BG00012 120 mg PO once daily (120 mg/day), 120 mg PO three times daily (360 mg/day), 240 mg PO three times daily (720 mg/day), or placebo. The study consists of 2 phases: a 24-week double-blind treatment phase followed by a 24-week, blinded, safety-extension phase in which all patients will receive some level of BG00012. The primary endpoint is the total number of Gd+ lesions over four MRI scans at weeks 12, 16, 20, and 24 (calculated as the sum of these four MRI scans). Secondary MRI endpoints include the cumulative number of new Gd+ lesions and the number of new or newly enlarging T2-hyperintense lesions at week 24 compared with baseline. Additional endpoints include: the number of new T1-hypointense lesions at week 24 compared to baseline, safety and tolerability, disability progression as measured by EDSS, relapse rate, and proportion of relapse-free patients.

Results: This paper will present details of the study design, as well as the baseline demographic and clinical characteristics of enrolled patients.

Conclusions: This dose-ranging study will determine the efficacy of BG00012 on brain lesion activity in patients with RRMS.

P575

A helper dependent adenovirus efficiently delivers bioactive FGF-II to the CNS

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We tested a FGF-II-expressing HD-Ad vector called STK120-GFP-FGFII in naïve mice focusing on the ability of FGF-II to induce stem cells proliferation and migration. We injected naive C57BL/6 mice in the cisterna magna with 10^8 transducing unit (t. u.) of STK120-GFP-FGFII; control mice received the "empty" STK120-GFP vector. Mice were sacrificed at 7, 14, 21 and 28 days post injection. We administered BrdU to the mice to mark all proliferating cells. Preliminary analysis showed ventricular enlargement in STK120-GFP-FGF-II-injected mice; this was evident one week post injection and persisted 4 weeks thereafter. We then performed BrdU staining by immunochemistry and counted BrdU positive cells near the lateral ventricles. STK120-GFP-FGFII-injected mice displayed a three-fold increase in BrdU positive cells as compared to control mice. This increase was already present one week after the treatment, and persisted at 2 and 3 weeks after injection, but disappeared 4 weeks after vector administration.

P576

Immunoablation using cyclophosphamide without haematopoietic stem cell rescue for refractory multiple sclerosis

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Objective: To assess safety and efficacy of very high dose cyclophosphamide (CYP) without hematopoietic stem cell (HSC) rescue for intractable multiple sclerosis (MS), as a realistic substitute for autologous HSC transplantation.

Background: Immunoablation without HSC rescue has been beneficial in other autoimmune diseases (eg, CIDP, SLE, myasthenia gravis) and may thus be a viable therapeutic option for intractable MS. No such data have been published. The aldehyde dehydrogenase mediated resistance of HSCs to CYP allows for reconstitution of a potentially advantageous naïve immune system.

Study Design: We initiated an IRB-approved study of ten patients with intractable MS, defined as having recurring relapses, worsening clinical deficits, and frequent contrast-enhancing lesions on MRI over 6 to 12 months in spite of conventional therapies with immunomodulators and immune suppressants. Patients will receive immunoablative doses of CYP 200 mg/kg divided over 4 days, similar to previously published studies. On day 10, patients will start granulocyte-colony stimulating factor (G-CSF, 5 µg/kg/day), until the absolute neutrophil count (ANC) rises to 0.5 x 10^9/L for 2 days. Following immunoablation, clinical, EDSS, laboratory and MRI follow-ups will occur at three to six month intervals over one year.

Case Report: A 23-year-old woman with relapsing MS for 3 years presented with ataxia, cognitive and behavior decline, and increasing burden of gadolinium enhancing lesions on serial brain MRIs. She had failed interferon-beta, glucocorticoids, and three courses of IV CYP (1000 mg/m^2). Immunoablation resulted in leukopenia (WBC trough of 44 x 10^6/L by day 11), and was > 0.5 x 10^9/L by day 15 (day 6 of G-CSF). No new neurologic symptoms or signs developed during and after the treatment period. We will show detailed longitudinal clinical, MRI, and laboratory metrics from this first in the series of our study subjects.

Conclusion: To our knowledge, this is the first published report of immunoablation in recalcitrant MS using high dose CYP without HSC rescue.