enhanced when the molecules were administered in viscous solutions: the dispersal area of pristine MNPs administered in saline solution with 3% sucrose, or with 3% or 6% polyethylene glycol, was significantly greater than that of pristine MNPs in saline solution only ($P<0.007$, $P<0.053$ and $P<0.011$, respectively). MRI monitoring of the clearance rate of dextran-coated MNPs showed that there was approximately 80–90% clearance from the brain by 40 days.

The authors conclude that dextran coating of MNPs and the use of high-viscosity infusion solutions improve the efficacy of CED in a rat model and might facilitate the use of CED for the administration of large particles, such as drug-loaded MNPs and gene-therapy-related products, in the treatment of brain tumors in humans.

Original article Perlstein B *et al.* (2008) Convection-enhanced delivery of maghemite nanoparticles: increased efficacy and MRI monitoring. *Neuro Oncol* [doi:10.1215/15228517-2008-002]

Varicella zoster virus contributes to relapse in patients with multiple sclerosis

Previous studies have indicated that reactivation of latent varicella zoster virus (VZV) might be associated with relapse in patients with multiple sclerosis (MS). Sotelo *et al.* examined patients with a definite diagnosis of relapsing–remitting MS to determine the role of VZV in the exacerbation of this condition.

All cerebrospinal fluid (CSF) samples from 15 patients with MS who were in the first week of a clinical relapse had a high content of VZV DNA (mean 204,489 ± 26,782 copies/ml) and contained large numbers of viral particles that were morphologically identical to VZV. Samples from these patients were negative for all other types of herpesvirus. The quantity of VZV DNA was much lower in the CSF samples of 19 patients in remission from MS than in those in relapse.

Similarly, all patients in relapse, but few patients in remission, had VZV DNA in their peripheral blood mononuclear cells. All 10 patients examined longitudinally had VZV DNA in their blood samples during the first week of follow-up and 9 patients had VZV DNA in the second week; only 4 individuals tested positive for VZV DNA (in small amounts) after ≥40 days.

The authors conclude that the presence of VZV in the blood and CSF of patients with MS who are in relapse and the decrease during disease remission indicate a direct role for VZV in the pathogenesis of MS relapse.

Original article Sotelo J *et al.* (2008) Varicella-zoster virus in cerebrospinal fluid at relapses of multiple sclerosis. *Ann Neurol* **63:** 303–311

Istradefylline reduces motor fluctuations in Parkinson's disease

The efficacy of levodopa therapy for Parkinson's disease (PD) declines with time, and some patients experience breakthrough motor symptoms as doses wear off. These motor fluctuations are caused by an overactive striatopallidal output pathway, so they could potentially be alleviated by blockade of A_{2A} adenosine receptors on striatopallidal neurons. To test this theory, LeWitt and colleagues investigated the effects of istradefylline, a selective adenosine A_{2A} receptor antagonist, in patients with PD who were receiving levodopa therapy.

A total of 195 patients in the US and Canada were randomly allocated to receive oral tablets of either istradefylline (40 mg daily; $n=129$) or placebo ($n=66$), for 12 weeks. Patients kept diaries to record episodes of inadequately controlled motor symptoms ('off time'); at baseline, all patients had ≥2 h (mean >6 h) of 'off time' per 24 h. During the 12-week study, daily awake time spent in the 'off' state decreased by 1.8 ± 2.8 h (28%) in istradefylline-treated patients and by 0.6 ± 2.7 h (10%) in placebo-treated patients ($P=0.005$). Improvements were observed by the second week after initiation of istradefylline and continued throughout the trial period. Although istradefylline-treated patients reported more time with dyskinesia than did placebo-treated patients, there was no difference between groups in the amount of dyskinesia described as troublesome. The study showed istradefylline to be safe and well tolerated.

These findings indicate that istradefylline shows promise for the control of breakthrough motor symptoms as commonly experienced by patients with advanced PD. The authors suggest that a neuroprotective effect of istradefylline might also reduce the progression of PD—an idea that warrants further investigation.

Original article LeWitt PA *et al.* (2008) Adenosine A_{2A} receptor antagonist istradefylline (KW-6002) reduces "off" time in Parkinson's disease: a double-blind, randomized, multicenter clinical trial (6002-US-005). *Ann Neurol* **63:** 295–302