

implies a substantial reduction in pertussis transmission in England and Wales. More complex pertussis models that incorporate different levels of immunity and age-specific vaccination schedules give qualitatively similar results.

In addition to the interepidemic interval, we explored other dynamic consequences of vaccination. The onset of mass vaccination coincided with a major change in the spatiotemporal patterns of pertussis incidence.<sup>5</sup> Vaccination was associated with a transition from spatially incoherent epidemics in the 1950s to geographically synchronised outbreaks in 1960s and 1970s with an almost 4-year period. Models support the hypothesis that this transition was caused by a substantial fall in transmission.<sup>5</sup>

Finally, we investigated the efficacy of vaccination by studying the pattern of fade-outs—ie, the frequency and duration of reports of no cases in individual locations (figure 2).<sup>3</sup> A very large increase in both number and duration of fade-outs occurred in the vaccine era, consistent with spatial synchronisation of epidemic troughs.<sup>5</sup> The importance of these observed changes in the fade-out structure very much depends on the frequency of mild or subclinical infections. In the absence of unequivocal evidence that the occurrence of symptomless infections radically increased after vaccination, the striking changes strongly indicate that vaccination has successfully reduced pertussis transmission.

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## Autoimmune T cells as potential neuroprotective therapy for spinal cord injury

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**Autoimmune T cells against central nervous system myelin associated peptide reduce the spread of damage and promote recovery in injured rat spinal cord, findings that might lead to neuroprotective cell therapy without risk of autoimmune disease.**

Secondary degeneration after spinal cord injury can cause disability beyond the severity of the primary insult. We have shown<sup>1</sup> that autoimmune T cells specific to myelin basic protein (MBP) of the central nervous system (CNS) can enhance the recovery of an experimentally crushed optic nerve.

We investigated the role of autoimmune T cells in the treatment of experimentally crushed rat spinal cords.

18 rats were deeply anaesthetised, laminectomised, and had their spinal cords at T7–T8 contused by a weight drop device.<sup>2,3</sup> Six of the rats were then injected intraperitoneally

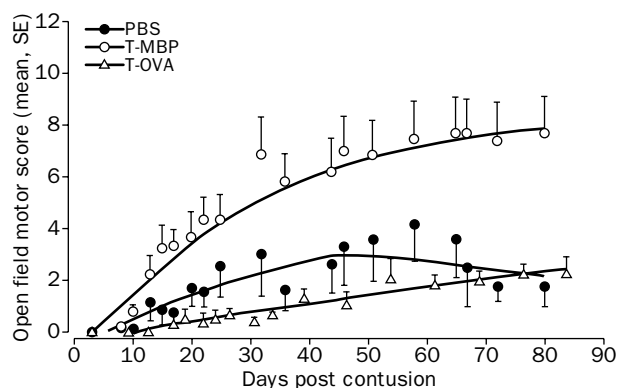


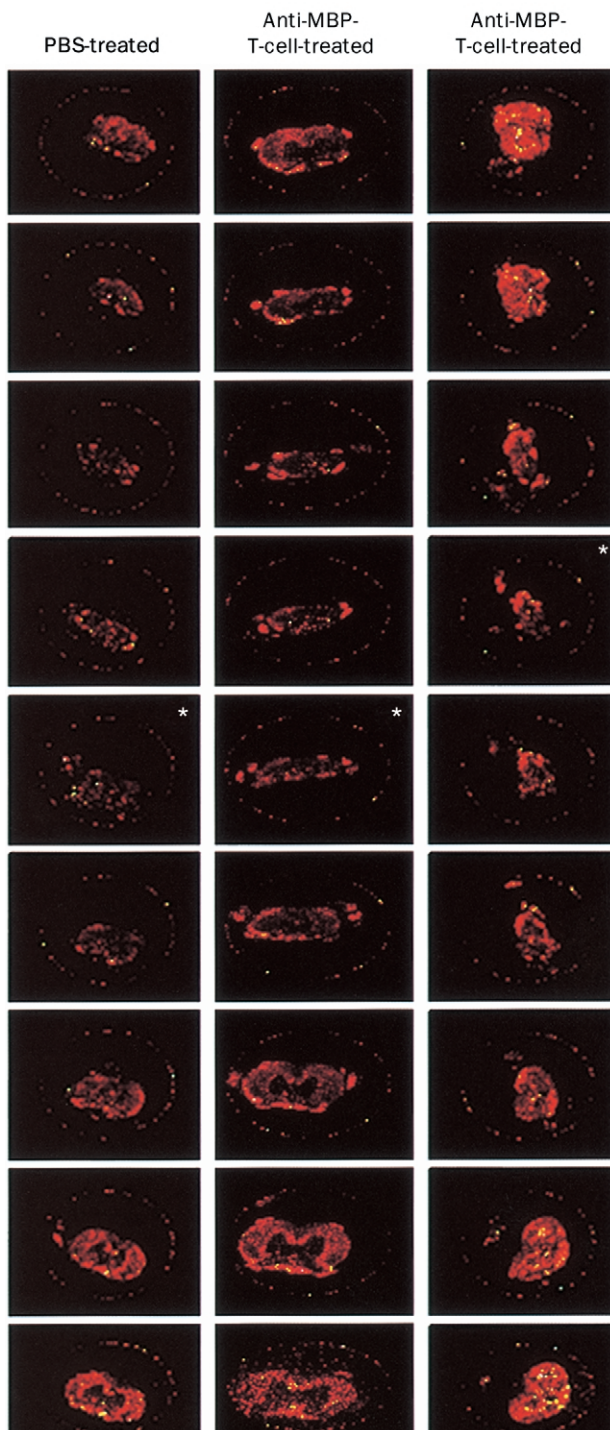
Figure 1: **Anti-MBP T cells enhance recovery of spontaneous motor activity after spinal cord contusion**

Following contusion and treatment with either cells or vehicle functional recovery over time was scored in an open field test on a scale of 0 (complete paralysis) to 21 (complete mobility)<sup>2</sup> by observers blinded to the treatment received by each rat. Mean values for each group (vertical bars SE) are shown. Differences between the group treated with the anti-MBP T cells and the other two groups, tested by repeated ANOVA, were significant ( $p < 0.05$ ).

with  $10^7$  anti-MBP T cells, six with  $10^7$  cells directed against the non-self antigen ovalbumin (OVA), and six with phosphate buffered saline (PBS). All the rats were paralysed immediately after the contusion (figure 1), but recovery began earlier in the rats treated with the anti-MBP T cells and, at all times from 11 days on, the anti-MBP T cell-treated group showed significantly greater locomotor recovery than did the controls. The mean maximum behavioural scores at plateau (1 month) were 1.5 (SE 0.8) for the PBS-treated group, 2.1 (0.2) for the anti-OVA T cell-treated control, and 7.7 (1.4) for the anti-MBP T cell-treated group (figure 1). Clinically, these scores showed an almost total lack of spontaneous motor activity in the controls, whereas the rats treated with the anti-MBP T cells could move all their joints and some could support their weight.

The amount and integrity of the neural tissues remaining in control and treated rats were assessed by diffusion weighted magnetic resonance imaging (MRI). Spinal cords of rats were excised 2 months after trauma and treatment and were immediately fixed and placed in MRI tubes. Nine axial slices, positioned around the site of lesion, were subjected to diffusion weighted multislice spin echo imaging (Nevo U, Hauben U, Yoles E, et al, unpublished data). The accumulated diffusion anisotropy in each slice (SAI) was calculated, and in each rat, the slice with the lowest SAI was defined as the lesion site. The maps demonstrate preservation of longitudinally ordered tissue at the lesion site of the anti-MBP T cell-treated rats. The loss of tissue at the site of injury in the control rat is much greater than that seen in rats from the anti-MBP T-cell treated group.

Images of axial slices from the spinal cords of rats who received anti-MBP T cells, by contrast with the controls, showed areas of diffusion anisotropy along the entire length of the cord and a continuous longitudinal structure (figure 2). The accumulated values of diffusion anisotropy at the centre of the site of injury (where diffusion anisotropy was at its lowest) in the anti-MBP treated group was two-fold higher than in the controls. The neuroprotective effect of the autoimmune T cells was further substantiated by immunohistochemical analyses using confocal microscopy; the anti-MBP T cell-treated rats showed well-organised spared neural tissue with few if any cysts, whereas the control rats showed a gap in continuity of the neural tissue and large cysts (Hauben E, Butovsky O, Nevo U, et al, unpublished data).



**Figure 2: Maps of diffusion-weighted MRI of the contused spinal cords**

Slice thickness was 0.5 mm, and slice separation 1.18 mm. Left to right images represent axial slices from head to foot. The figure shows representative maps of two spinal cords of rats treated with anti-MBP T cells and one spinal cord of a rat treated with PBS. Colours correspond to anisotropy values (A); bright colours mark pixels with high values.

Our results show that a single post-injury injection of autoimmune T cells directed against the CNS myelin protein MBP, promotes long-lasting recovery after severe contusion of the spinal cord in rats.

Adaptive immunity represents the body's system of defence against foreign dangers.<sup>4</sup> Our studies now show, however, that the adaptive T-cell immune response can be protective even when there is no invasion by foreign pathogens. In this case the T cells, rather than being directed

against invaders, are specifically directed against tissue self-antigens.<sup>5</sup> The striking effect of the autoimmune T cells suggests that therapeutic neuroprotection may be achieved by development of the autoimmune T cell model, using suitable autologous autoimmune T cells devoid of the ability to cause permanent autoimmune disease.

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## Structured treatment interruptions to control HIV-1 infection

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**Structured treatment interruptions progressively lowered the rate of viral rebound in some HIV-1 infected patients. This approach should be explored as an alternative to continuous antiretroviral therapies.**

Eradication of HIV-1 by therapeutic intervention seems to be an elusive goal.<sup>1</sup> Even when highly active antiretroviral therapies (HAART) result in persistently undetectable viral load, withdrawal of the treatment is usually followed by a rapid viral rebound.<sup>2,3</sup> We have described a patient in Berlin who was given hydroxycarbamide, didanosine, and a protease inhibitor before complete seroconversion as shown by western blot, and whose treatment was interrupted twice before permanent discontinuation.<sup>4</sup> 2 years after treatment was stopped, HIV-1 RNA in the plasma of this patient was still below the limit of detection (<500 copies/mL). These findings suggest that structured treatment interruptions of combinations based on hydroxycarbamide contributed to the control of HIV-1 replication in the absence of drugs.<sup>4</sup>

To test the feasibility of structured treatment interruptions in a prospective study, three antiretroviral-naïve patients were treated with hydroxycarbamide-containing HAART at various times after complete seroconversion, as shown by western blot. The three patients were heterogeneous in terms of initial viral load (16 130 copies/mL, 21 845 copies/mL, and 719 000 RNA copies/mL) and CD4-cell count (508/μL,