no neck stiffness. A distally accentuated weakness of the left arm (grade 3/5) was found. Furthermore, he presented with spastic weakness of both legs that was more pronounced on the left (grade 3/5 on the left, grade 4/5 on the right). Deep muscle reflexes were brisk in the left arm and in both legs, but pyramidal signs could not be elicited. There was decreased sensation to light touch and pinprick in the legs without a clearcut level.

Whereas visual evoked responses and nerve conduction velocity of motor and sensory nerves were normal, motor evoked potentials to the feet induced by transcutaneous magnetic stimulation of the motor cortex showed a 50% reduction of amplitude on the left and a longer latency on the right. The somatosensory evoked potentials derived from the tibial nerve showed a reduction in amplitude on the right.

T2 weighted MRI of the brain showed two hyperintense lesions with a diameter of about 1 cm, one localised in the centrum semiovale and the other one in the brain stem near the lemniscus medialis, both on the left side. After intravenous administration of contrast medium no disruption of the blood-brain barrier was detectable. Magnetic resonance imaging of the cervical and thoracic spine showed a swelling of the spinal cord at level C 2/3 and Th 2. After intravenous administration of the contrast medium an enhancement was visible in both localisations as a sign of an acute inflammatory process. Routine laboratory tests were normal except for slightly raised erythrocyte sedimentation rate and liver enzymes. Serological testing by enzyme linked immunosorbent assay (ELISA) showed antibodies against varicella zoster virus of the IgG and IgM type and also IgG antibodies against measles virus but no anti-measles IgM antibodies. All other serological tests for antibodies against neurotropic viruses, especially herpes simplex virus, cytomegalovirus, mumps virus, coxsackie viruses types B 1–5, adenoviruses, influenza, and parainfluenza viruses as well as *Borrelia burgdorferi*, were negative or did not give evidence of a recent infection.

Cerebrospinal fluid cytology disclosed a subacute inflammatory CSF cell syndrome with transformed lymphocytes and plasma cells. Whereas the albumin content was normal (18·4 mg/dl), the IgG (4·2 mg/dl) was slightly raised. The IgG index calculated according to Delpech and Lichtblau was 0·70. Oligoclonal IgG bands were present in CSF only. Repeated lumbar taps did not show major changes in the findings. Detection of varicella zoster virus DNA by the polymerase chain reaction could not be achieved in blood or CSF. Antibodies of the IgG type against varicella zoster virus and measles virus were slightly raised giving titres of 1 : 40. Differentiation of CSF antibodies by isoelectric focusing and the immunoblot technique showed that about 20% of the oligoclonal CSF IgG was directed against the nucleocapsid protein of measles virus. Autochthonous synthesis of varicella zoster virus specific antibodies could not be detected.

Suspecting an acute varicella zoster virus myelitis, we initially treated with acyclovir (30 mg/kg body weight/day in three doses). Symptoms resolved under this treatment and intensive physiotherapy. The patient was discharged with mild residual symptoms consisting of a spastic, atactic gait after 21 days. Eight weeks after the first admission he presented with a left optic neuritis. Visual evoked potentials could not be elicited on the left whereas they were normal on the right. There were no other neurological symptoms or signs apart from the residual gait disturbance, which had greatly improved in the meantime. After one course of high dose prednisolone (1000 mg/day intravenously for five days) visual acuity returned to normal. The subsequent course was stable; repeated cranial MRI did not show any newly enhancing lesions.

According to the criteria of Poser *et al*[4] this patient had clinically definite, laboratory and MRI supported, multiple sclerosis. Five days before the second bout he developed acute varicella. In considering the time course, an immune mediated postinfectious encephalomyelitis is highly unlikely as it should have become symptomatic not earlier than the second week after the onset of the rash. The failure to detect varicella zoster virus DNA by polymerase chain reaction in CSF and the lack of autochthonous varicella zoster virus specific oligoclonal IgG production in CSF while oligoclonal IgG was present is strong evidence against direct viral infection of the CNS. The presence of oligoclonal IgG in the CSF directed against measles virus proteins is a common finding in patients with multiple sclerosis. The close temporal association between the hitherto more severe second bout and the varicella infection suggests precipitation of an acute exacerbation of pre-existing multiple sclerosis by varicella. No specific virus has been consistently implicated in the precipitation of exacerbations in patients with multiple sclerosis, with the exception that a significant correlation between increases in adenovirus titre associated with upper respiratory tract infections and major relapses has been shown.[2] It is unlikely that the precipitation of exacerbations occurs non-specifically during any infection as bacterial infections and those often affecting the urinary tract in patients with multiple sclerosis do not lead to an increased rate of episodes.[1]

As a possible mechanism to explain our finding, interferon-γ has been shown to have a deleterious effect on the clinical course of multiple sclerosis in that it precipitates exacerbations.[5] By inducing the release of cytokines such as interferon-γ, viral infections may enhance an autoreactive response to CNS antigens via upregulation of adhesion and HLA-molecule expression as well as activation of effector cells such as macrophages. Although the pathogenetic background still remains obscure, this case shows that precipitation of an exacerbation of pre-existing multiple sclerosis by chickenpox is possible.

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Interferon-α may benefit steroid unresponsive chronic inflammatory demyelinating polyneuropathy

Although controlled studies have shown the efficacy of plasma exchange, corticosteroids, and intravenous immunoglobulin (IVIg) in chronic inflammatory demyelinating polyneuropathy (CIDP), many patients do not achieve a complete and long term remission and some patients do not respond at all to these treatments.[1]

We report on two patients with CIDP, unresponsive to corticosteroids, azathioprine, or cyclosporin, who showed a partial and short lived response to IVIgs but made a complete and sustained recovery after treatment with interferon α-2a.

The figure summarises the clinical courses of patients. The disability was assessed on the Rankin scale.[1]

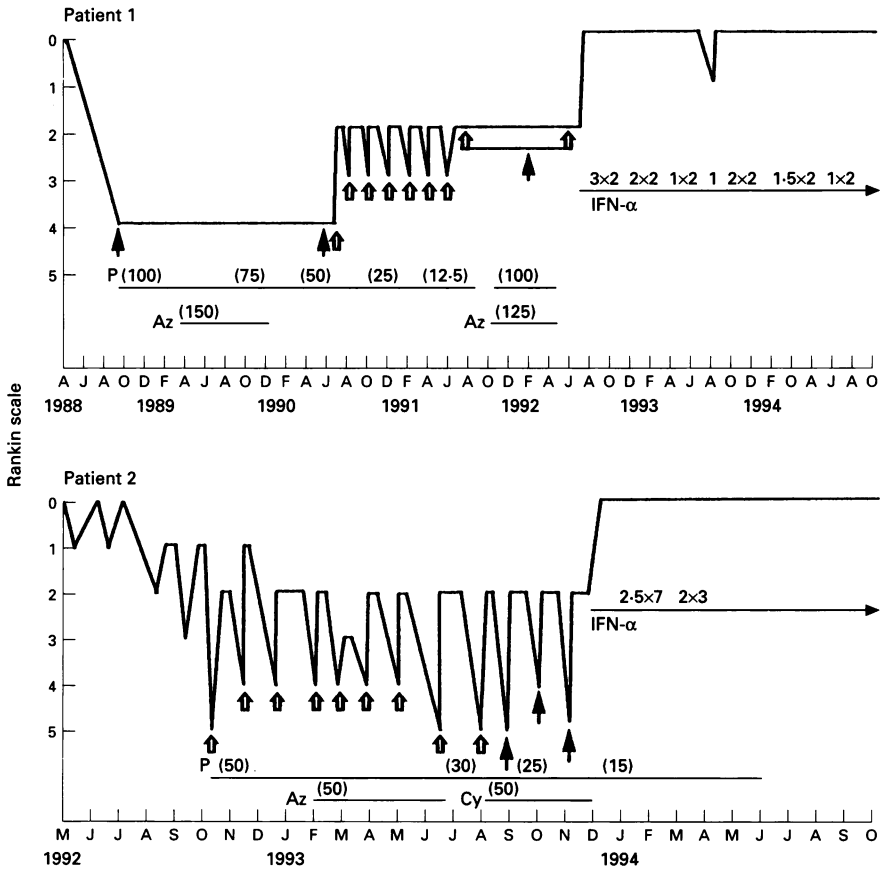
Patient 1 was a 27 year old girl admitted in June 1990. In 1988 she had a progressive limb weakness that had evolved over six months. A diagnosis of CIDP was made in another neurological institute and the patient was treated with prednisone, plasma exchange, and azathioprine with poor response.

The patient showed severe, symmetric weakness of proximal and distal muscles, normal sensation, and absent tendon reflexes. Cranial nerves were unaffected. Routine haematological examinations and serum and urine immunoelectrophoresis gave normal results. Serological tests for Lyme disease and HIV were negative. The protein content of CSF was 60 mg/dl. Nerve conduction studies showed slightly reduced motor conduction velocities with multiple conduction blocks. Sural nerve biopsy was normal.

The patient was treated by plasma exchange without any effect. She was then given IVIg at a dosage of 0·4 g/kg/day for five consecutive days and showed considerable improvement. After that, six relapses occurred (the mean time between relapses was five weeks) and on each occasion reinstitution of IVIg was followed by a similar improvement.

Subsequently, we started intermittent treatment with IVIg (1 g/kg for one day every four weeks), which was successful in maintaining the maximal level of improvement. During the maintenance period additional treatments with corticosteroids, plasma exchange, and azathioprine were given, but the frequency of IVIg treatment was not altered, deterioration occurring each time we tried to prolong the interval between infusions to more than five weeks.

In January 1992 the patient noticed a



Clinical course of patients 1 and 2. ⇧ = high dosage intravenous immunoglobulins (HIG); ⇧⇧ = HIG maintenance; ⬆ = plasmapheresis; P = prednisone, (alternate day dosage (mm) in parentheses); A = azathioprine; Cy = cyclosporin (daily dosage in parentheses); IFN-α = interferon-α (weekly dosage in million IU).

temporary improvement during and after a flu like syndrome. In July 1992 solo treatment with interferon-α-2a (Roferon-A) at a dosage of 3 million international units (MIU) twice weekly was begun. On the third day after the first injection a dramatic improvement was seen and during 11 days the patient progressively recovered to normal. Serial nerve conduction studies showed progressive reduction of conduction blocks. Seven days after the reduction of interferon-α to 1 MIU/week, progressive weakness of distal muscles occurred that paralleled an increase in multiple conduction blocks. Reinstitution of interferon-α-2a treatment at a dosage of 2 MIU twice weekly, produced a complete recovery within six days. Again the dose of interferon was gradually reduced to 1 MIU twice weekly, without clinical changes.

Only minor adverse effects, such as fever and arthromyalgia, were seen during interferon treatment.

Patient 2 was a healthy 3 year old boy who developed a waddling gait and muscle pain in his legs 20 days after an upper respiratory tract infection. The patient had recovered spontaneously after 15 days. During the next three months he had another three episodes of leg weakness lasting 10–15 days. Brain and spinal cord MRI was normal; electrophysiological studies showed delayed motor conduction velocity with multiple conduction blocks in all the nerves tested and normal sensory conduction velocities. The CSF contained 96 mg/dl protein and 3 white blood cells/ml, but no oligoclonal bands.

During the fifth attack the child became unable to walk unaided and was admitted to our neurological department. He was treated with IVIg at a dose of 1 g/kg daily for two days and prednisone (at a dose of 50 mg every other day) and after three days he regained the ability to walk. Neurography showed disappearance of conduction blocks in two of three motor nerves. Twenty days later the boy had another relapse. Again treatment with IVIg improved motor symptoms in a few days. In the next 15 months he showed relapses every 13 to 20 days despite treatments with azathioprine and cyclosporin. All the episodes responded to IVIg. During three relapses the patient was treated with plasma exchange and showed improvement comparable with IVIg treatment. Treatment with interferon-α-2a (Roferon-A) (2·5 MUI/day)) was given. After this treatment the child regained normal strength within 15 days. The dose of interferon-α was reduced to 2 MIU twice a week after three months. The patient showed no relapses during the subsequent months and no adverse effects were seen. Neurography performed two months after interferon treatment showed improvement of motor conduction velocity in all nerves with pronounced reduction of conduction blocks.

On the basis of the research criteria for the diagnosis of CIDP[2] our patients were affected by "probable CIDP". Despite a good response to IVIg, these patients were still moderately disabled and frequent infusions were needed. In 1992 Engel *et al*[3] described a patient with long lasting CIDP unresponsive to corticosteroids, azathioprine, cyclosporin, plasma exchange, and IVIg, who showed pronounced improvement with interferon-α treatment. This finding led us to the use of interferon in our patients.

Interferon-α treatment resulted in a dramatic and long term recovery. We doubt that this response was fortuitous, because (*a*) both patients showed a pronounced improvement a few days after starting interferon-α and this result was never achieved with other treatments; (*b*) no relapse occurred during full dosage interferon-α treatment whereas before this the patients had had a relapsing course over a long period, despite immunosuppressive treatments; (*c*) patient 1 deteriorated on reducing interferon-α to 1 MIU a week and promptly responded to a higher dose, suggesting a dose-response effect.

The mechanism by which interferon induced an improvement in our patients is uncertain. Interferons exert complex immunomodulator effects and there is evidence that interferon-α may both improve or worsen autoimmune disease.[4] The recent finding that interferon-α may benefit patients affected by multiple sclerosis and that the production of lymphocyte interferon-γ is reduced by this treatment, suggests that interferons may play a central part in the pathogenesis of demyelination in both the central and the peripheral nervous system.[5]

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Kava and dopamine antagonism

Kava is a drink widely used for its calming and tranquilising properties by the native population in the islands of the south Pacific.[1] The beverage is prepared from the roots of the kava plant (*Piper methysticum*); Besides its widespread social use it is also a ceremonial drink, and heads of state have been reported to drink kava during welcome