IFN and AZA treated groups without differences between the two treatments, whereas it was unchanged in the NT group. The EDSS remained stable in the three groups (table). Five of 11 patients treated with IFN had flu-like symptoms on one or more occasions, whereas no side effects occurred in the other two groups.

No significant differences in the HD scores and quality of life profile were found between the three groups at entry. At 6 (data not shown) and 12 months the mental health composite score significantly increased in patients treated with AZA compared with the patients treated with IFN, mainly due to the increase in role limitation for emotional reasons item; no significant differences between the NT group and actively treated groups were seen. No significant changes in HD scores in the three groups were found at 12 months. These results suggest that both AZA and IFNβ-1b are effective in reducing relapse frequency in patients with RRMS. The treatment effect on quality of life has been rarely investigated, with conflicting results: no significant change after 1 year of IFNβ-1b treatment was found by Schwartz *et al*,[4] whereas an improvement on physical items after 5 years was reported by Rice *et al*.[5] In our study, the impact on quality of life was better in patients treated with AZA than in those treated with IFN, mainly due to the improvement in mental score. A direct effect of the drugs on the CNS seems unlikely: no symptoms of neurotoxicity were found in either treatment group and no patients developed depression according to the HD scale. Most likely the improvement of quality of life in patients treated with AZA might be related to different tolerability or to differences in treatment schedules, resulting in a more pronounced and persistent perception of the disease in patients treated with IFN. Due to the few patients, the results of this study need to be verified by a larger randomised comparative trial.

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Unilateral caudate head lesion simulating brain tumour in X-linked adult onset adrenoleukodystrophy

The appearance of X-linked adrenomyeloneuropathy (AMN)/adrenoleukodystrophy (ALD) on MRI is usually specific, with bilateral symmetric areas of white matter abnormality surrounding the posterior horns of the lateral ventricles with various degrees of atrophy of the spinal cord.[1] Our patient with AMN, however, showed a lesion in the right caudate head simulating a brain tumour, which has not been a feature in this disease.

At the age of 25 the patient started to have progressive spastic paraparesis and mild ataxia with genitourinary dysfunction (urge urinary incontinence and erectile dysfunction).[2] On admission to our hospital at the age of 34, T2 weighted MR images showed small lesions in the bilateral internal capsule although no abnormality was seen in the spinal cord. Nerve conduction studies and the sural nerve biopsy showed evidence of peripheral nerve involvement. A low serum cortisol response to intravenous adrenocorticotropic hormone and increased concentration of plasma very long chain fatty acids were consistent with a diagnosis of AMN. Three years later he showed marked emotional lability. T2 weighted MRI showed a high signal mass lesion in the right caudate head and the ipsilateral anterior internal capsule which simulated an intracranial tumour, without marked demyelination in the surrounding deep white matter (fig 1). A year later he became wheelchair bound, apathetic, and demented. Brain MRI showed right sided dominant white matter abnormalities and atrophy of the spinal cord. Three years later he died of respiratory infection and necropsy was performed. Pathological examination showed frontotemporal cortical atrophy with diffuse white matter demyelination including bilateral internal capsules, where astrocytes proliferated and lipid laden macrophages infiltrated around the small vessels. Neurons were moderately shrunken and the neuropil showed tissue rarefaction. Demyelination was also seen in the cerebellar white matter. The caudate head showed bilateral but right side dominant atrophy, where neuronal loss and tissue rarefaction with fibrillary gliosis (spongy state) were seen (fig 2).

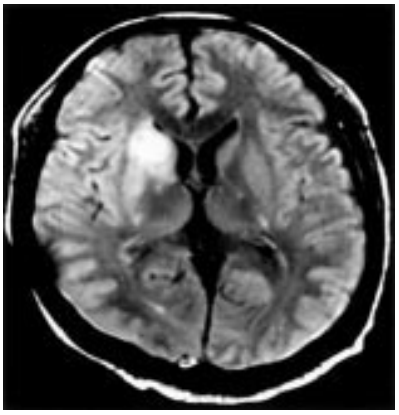

Figure 1 Brain MRI of the patient at the age of 37. T2 weighted MR images showed a high signal mass lesion in the right caudate head and the ipsilateral anterior internal capsule which simulated an intracranial tumour, without marked demyelination in the surrounding deep white matter.

Previous reports of X-ALD/AMN showed occasional unilateral basal ganglia involvement. Afifi *et al* reported on a 4.8 year old boy whose MRI showed a right anterior white matter lesion extending into the ipsilateral putamen and the thalamus.[3] Close *et al* described an 8 year old boy who had a left occipitotemporal white matter lesion extending into the ipsilateral thalamus on MRI.[4] However, the imaging pattern in our patient is unique because of the high signal mass lesion in the right caudate head and the ipsilateral anterior internal capsule without marked demyelination in the surrounding white matter, falsely suggestive of a brain tumour. There are also other demyelinating disorders simulating brain tumour which include multiple sclerosis.[5] The findings indicate that plasma very long chain fatty acid

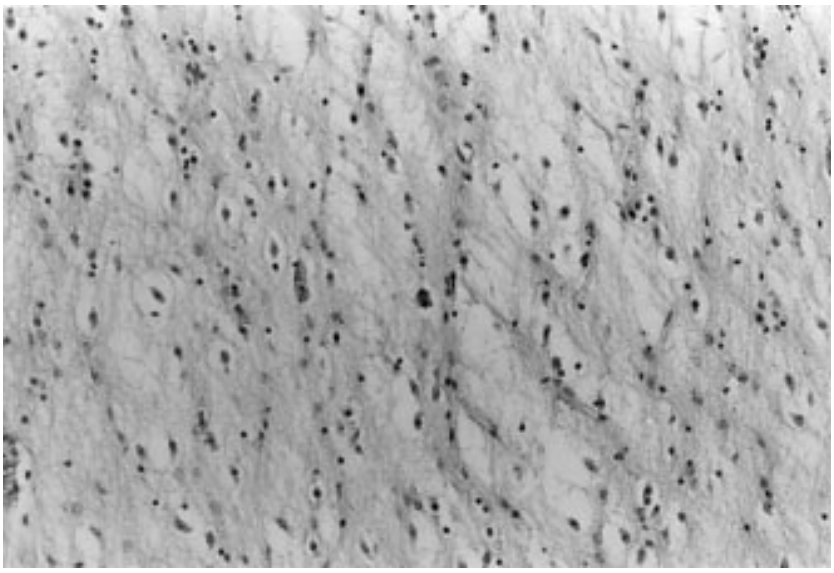

Figure 2 Microscopic section of the right caudate head (haematoxylin-eosin staining, originally×50). This shows neuronal loss and tissue rarefaction with fibrillary gliosis, presenting as spongy with little inflammation.

concentrations should be measured in patients with unexplained basal ganglia abnormalities on MRI.

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Lymphadenopathy in patients with multiple sclerosis undergoing treatment with glatiramer acetate

Glatiramer acetate (GA)—formerly known as copolymer 1 or COP-1—has been shown to reduce the frequency of relapses and disease activity and burden as measured by MRI in patients with relapsing-remitting multiple sclerosis (RR-MS).[1] The mechanism of action is thought to involve MHC-II blockade[2] and the induction of a Th2/Th3 cytokine response.[3] Peripheral blood mononuclear cells from patients with multiple sclerosis and healthy controls proliferate in reponse to GA in vitro.[4] Therefore GA seems to have both immunostimulatory and immunomodulatory potential.

In our centre 27 patients with relapsing-remitting or relapsing-progressive multiple sclerosis were treated with 20 mg subcutaneous GA daily for 3 years as part of an open label multicentre study. Safety evaluation and expanded disability status scale (EDSS) rating were performed every 3 months and in the 3rd year every 6 months and when clinical relapses occurred. Relapses were defined according to Poser criteria and annual relapse rates were calculated for the 3 year study duration and a 2 year prestudy period. As two patients reported generalised tender swelling of lymph nodes spontaneously in temporal relation to the beginning of GA injections special attention was paid to the symptom and regular assessment of regional lymph nodes was performed in all patients. Only if patients reported symptoms such as tenderness or pain, was the diagnosis of lymphadenopathy made. All patients completed the full 3 years of the study. In one patient with generalised lymphadenopathy a lymph node biopsy was taken to rule out malignancy. As controls patients who were routinely treated with IFN-β injections at our multiple sclerosis outpatient clinic were also examined for lymphadenopathy.

In nine out of 27 patients lymphadenopathy occurred 1 to 15 months after initiating GA treatment and persisted for the study (treatment) duration. There were no significant differences between the groups with and without lymphadenopathy in their mean age, disease duration, EDSS scores, and annual relapse rates at the beginning of the study. The size of the lymph nodes ranged from 2 to 5 cm and lymphadenopathy was considered mild to moderate in eight patients and severe in one patient. In seven out of the nine patients lymphadenopathy was restricted to inguinal lymph nodes and in two patients it was generalised. Serological and haematological routine diagnostics of peripheral blood were normal. The lymph node biopsy in one patient with severe generalised lymphadenopathy showed strong immune stimulation with lymphofollicular hyperplasia but no atypical cells (thus ruling out malignancy). Lymphadenopathy did not necessitate the discontinuation of GA treatment. The examiners were reassured that all patients used a good (sterile) injection technique. In the control patients no lymphadenopathy was detected.

When analysing annual relapse rates, a significant reduction of the mean annual relapse rate was found under GA treatment. The annual relapse rate decreased from 1.8/year to 0.33/year and from 1.5/year to 0.54/year in the group of patients with and without lymphadenopathy respectively. When comparing annual relapse rate for both patient groups the difference did not reach significance (Mann-Whitney *U* test, p=0.076) with a trend to a slightly favourable response in the group with lymphadenopathy. Although in the group with lymphadenopathy no patient showed an increase in relapse rate, three patients in the group without lymphadenopathy did. In both groups of patients no significant change in median EDSS over the 3 years of the study was noted (table 1).

The frequency of lymphadenopathy found in this study (nine out of 27 patients) is significantly higher than that reported in the postmarketing surveillance of GA (55 reports of lymphadenopathy out of about 30 000 reports of other adverse events). The lymphadenopathy in our study was mild to moderate, not accompanied by changes in routine laboratory indices, and persisted as long as the GA treatment was continued. In seven out of nine patients lymphadenopathy remained localised to the draining lymph nodes. Lymph node swelling receded and reappeared depending on injection site. Lymphadenopathy did not necessitate discontinuation of GA treatment. In one patient with generalised lymphadenopathy a biopsy was performed to rule out malignancy. The patient was then continued on GA without further problems and remained relapse free; GA injections were stopped 1 year after the end of the study, due to pregnancy, and lymphadenopathy resolved completely within 4 weeks.

Lymphadenopathy, if not due to malignancy, is a clinical sign of immune activation and has not yet been reported as an adverse event of GA treatment in the literature. The effect might be due to direct stimulation of T cells in vivo as GA has been shown to induce mRNA expression of IL-2 and T cell proliferation in vitro.[4] In previous studies immunostimulatory cytokines such as IFN-γ or viral infections worsened the clinical course of multiple sclerosis whereas immunosuppression (for example, mitoxantrone, cyclophosphamide) was beneficial.[5] It will be interesting to study further whether lymphadenopathy related to GA is associated with alteration of the clinical outcome measures of multiple sclerosis. The cohort of patients with lymphadenopathy did not show a significant difference in annual relapse rate or EDSS compared with patients without lymphadenopathy, but the small sample size per group should be taken into account. Glatiramer acetate induces clinical signs of immune stimulation (lymphadenopathy) in a subgroup of patients with multiple sclerosis that is not associated with clinical worsening. The finding is therefore interesting with regard to the potential mechanism of action of GA in vivo. Larger numbers of patients need to be examined to determine whether lymphadenopathy in patients under GA treatment is associated with distinct immunological markers—for example, MHC-II type or cytokine secretion pattern.

Clinical data of patients with multiple sclerosis treated with glatiramer acetate

	Annual relapse rate at start	*Annual relapse rate in study*	*EDSS at start of study*	*EDSS at end of study*
Lymph node swelling	1.8 (1–3.5)	0.33 (0–1)	2.5 (0–3.5)	2.5 (0–3.5)
No lymph node swelling	1.5 (1–3.5)	0.54 (0–1.8)	2.5 (1–5)	3 (0–6.5)

Values are mean (relapse rate) or median (EDSS) (range).

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