disease or Alzheimer's-type neuropathological changes, we suppose that the investigation of the catabolic system of Aβ is important for four reasons. Firstly, it links to elucidation of the mechanism of accumulation of Aβ. As NEP is thought to be a main peptidase which accounts for the degradation of Aβ in the brain,[1] it is necessary to examine the influence of the NEP gene on the severity of the senile plaques and dystrophic neurites to search for a role of clearance of Aβ in the deposition of Aβ. Secondly, this research contributes in clarifying a role for senile plaques and dystrophic neurites in the development of Alzheimer's disease. Thirdly, the detection of key molecules in the degradation of Aβ might directly lead to the treatment of Alzheimer's disease. Fourthly, recent analyses disclosed that families with late onset Alzheimer's disease are linked to genetic markers near the insulin degrading enzyme gene, which is thought to be one of the catabolic enzymes of Aβ.[6] Genes of the degradating enzymes of Aβ such as the NEP gene still remain potential risk factors for sporadic Alzheimer's disease. The examination of other polymorphisms in the NEP gene or multivariate analysis taking in the related gene except ApoE which modifies the processing of Aβ might detect potential correlation of the NEP gene with Alzheimer's disease.

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Human T lymphotropic virus type I (HTLV-1) associated myelopathy acquired through a liver transplant

Subacute myelopathy (HAM/TSP) is the main neurological manifestation of human T lymphotropic virus type I (HTLV-1) infection.[1] This virus is endemic in central Africa, Caribbean countries, and Japan. It is transmitted through sexual contacts, during lactation, and by blood transfusions. The risk of seroconversion after blood transfusion is 40%–60%. Around 5% of the carriers will develop clinical manifestations; only 0.3% of them will have a myelopathy. Inmunosupresion enhances the risk of infection, reduces the latency, and accelerates the clinical pictures. We are reporting the first documented case of HTLV-1 infection through an organ transplantation in a western country. In another organ recipient the vehicle of the virus was the blood transfused during the surgical procedure.[2]

A 44 year old woman developed alcoholic cirrhosis and hepatocarcinoma. On 5 October 1998, she received a liver transplant followed by cyclosporin treatment (175 mg/day). The donor was an apparently healthy young man who died after brain injury. Eighteen months later, the patient complained of progressive weakness in her legs. In the next 3 months a rapidly evolving paraparesis with a T6 sensory level, pyramidal signs, and bladder dysfunction became evident. She was admitted to another hospital. The CSF contained 37 white cells/ml, 93 mg/ml protein, and 43 mg/ml glucose. Serological tests for neurotropic virus were negative. On T2 weighted MRI a diffuse hypersignal of the cervicothoracic spinal cord was seen. The rest of the data from an extensive investigation were non-contributory. She was transferred to our institution on 3 August 2000. Other than a complete paraplegia no neurological abnormalities were found. Somatosensory evoked potentials after median nerve stimulation were normal but they were abolished after posterior tibial nerve stimulation. In the CSF there were 9 white cells/ml, 133 mg/ml protein, and 43 mg/dl glucose. Serological tests for HTLV 1 (enzyme linked immunosorbent assay (ELISA) and western blotting) were positive in blood and CSF, and the polymerase chain reaction was positive in blood. Tests were negative for HTLV 2 and VIH. The patient received a pulse of intravenous methylprednisolne (1g/day/5 days) and a course of α-interferon (3 MU/day/1 month)[3] without any improvement in her neurological status.

We have conducted a retrospective serological survey for HTLV 1 antibodies in archival blood samples from the patient before the transplantation, from the liver donor, and from the blood donors. All the samples were negative except those from the liver donor. He was a multiorgan donor (both kidneys, liver, heart, and corneas). A follow up of all the recipients is in progress.

The prevalence of HTLV-1 infection in the endemic areas is between 3% and 30%. In western countries it is less than 1%.[1] Despite of this low prevalence, several European countries (France, Holland, Sweden, Denmark, Luxembourg) and the United States have introduced a systematic search for HTLV-1 antibodies in their blood banks. Furthermore, in France the test for HTLV-1 infection is mandatory in all organ donors. In Spain, a serological survey conducted among 23 000 blood donors in 1992 detected only one suspected, subsequently not proved, carrier. Consequently, a routine test for HTLV-1 was not implemented. However, an ad hoc national registry reported 24 cases in Spain up to 1994.[4] Since then, three further cases have been found (V Soriano, personal communication). In Japan, Nakamura *et al*[5] reported that 15 out of 153 recipients of renal transplants were HTLV-1 positive. They did not develop HAM/TSP or any HTLV-1 related disorder during a follow up of 1 to 10 years. By contrast, the case we are reporting here indicates that HTLV-1 infection may have devasting consequences for some immunocompromised organ recipients. This emphasises the necessity for a systematic survey of its antibodies in all potential donors despite the low current prevalence of HTLV-1 infection in western countries.

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Relation between the high production related allele of the interferon-γ (IFN-γ) gene and age at onset of idiopathic Parkinson's disease in Japan

Although the pathogenesis of progressive degeneration of nigrostriatal dopaminergic neurons in Parkinson's disease remains uncertain, cytokines are thought to contribute to the development of the disease.[1] Interferon (IFN)-γ is one of the Th1 cell derived multifunctional cytokines and seems to influence neuronal differentiation and to increase in inflammatory and neurodegenerative diseases.[2] Immunohistochemical studies showed an increase of IFN-γ expression in nigral astrocytes of patients with Parkinson's disease.[3] This increase of IFN-γ concentration may be a trigger for the disease or a compensatory response. It was reported that IFN-γ producing capacity in whole blood cultures of untreated parkinsonian patients decreased compared with sex and age matched healthy controls.[4] This supports the idea that IFN-γ may increase in Parkinson's disease as a compensatory response. Concerning genetic polymorphisms in the IFN-γ gene, the production of IFN-γ measured in peripheral blood mononuclear cell cultures may correlate with dinucleotide CA repeat polymorphism in the first intron of the IFN-γ gene.[5] In vitro production of IFN-γ is higher in

people homozygous for allele 122 (12 CA repeats, named allele 2 by Pravica *et al*[5] and allele 6 by Awata *et al*[6]) than in those of other genotypes.[5] Therefore, we investigated the CA repeat polymorphism of the IFN-γ gene in 170 patients with idiopathic Parkinson's disease (102 women and 68 men, aged 64.2 (SD 9.7) years; onset, 55.5 (SD 10.6) years; disease duration 8.7 (SD 5.2) years). As controls, 157 healthy people were selected from the annual health examination at a city clinic. The control group was matched for age (mean: 62.5 (SD 8.7) years), sex ratio (98 women and 59 men), and birth place (Kyoto and Osaka prefectures) with the patients. All participants were Japanese. The study protocol was approved by the institutional ethics committees and informed consent was obtained from every participant. The CA repeat polymorphism was analyzed according to a previous report.[6] The result is shown in table 1. Using χ^2 analysis (combined rare alleles "116", "118", "130", and "132"), no significant difference was found in allele distribution between the Parkinson's disease and control groups (p=0.86). When patients were divided into two groups (early onset and late onset disease), pc was obtained by multiplying the p value by two. No significant difference was found between patients with early onset Parkinson's disease and controls (pc=0.23) or between those with late onset Parkinson's disease and controls (pc=1.17). However, the allele distribution was significantly different between early onset (<50 years) and late onset (≥50 years) disease (χ^2=14.3, df=5, pc=0.028). The frequency of allele 122 was lower in those with early onset Parkinson's disease than in those with late onset Parkinson's disease. Carriership analysis also showed a low allele 122 carrier frequency in patients with early onset compared with late onset disease (χ^2=4.62, df=1, pc=0.039). Although the genetic polymorphism of IFN-γ does not seem to be a risk factor for Parkinson's disease, a lack of high producer allele 122 may affect the onset of disease. The allele 122 may be part of a haplotype that also includes functionally relevant polymorphisms. Our findings support the idea that the increase of IFN-γ concentration in the brain of patients with Parkinson's disease might be a compensatory response rather than a trigger of the disease. Thus, IFN-γ might be helpful in delaying the progress of the disease.

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Autonomic dysreflexia due to neurogenic bladder dysfunction; an unusual presentation of spinal cord sarcoidosis

Clinical involvement of the CNS in sarcoidosis is seen in about 5% of patients.[1] The most common affected sites are the basal leptomeninges and the region of the floor of the third ventricle. However, primary involvement of the spinal cord is much less common.[1] It may cause serious neurological deficits below the affected level of the lesion. Here we describe a case of spinal cord sarcoidosis with an unusual presentation: autonomic dysreflexia due to neurogenic bladder dysfunction.

A 42 year old woman began to have a slowly progressive spastic gait, left hand numbness, urinary urgency/frequency, and voiding difficulty which worsened gradually for a year. She underwent C2–7 laminoplasty for a relief of C4–6 cervical disc herniation where mild cord swelling was present. However, her gait difficulty ameliorated only for 2 weeks. Two months later she became unable to walk without an aid. Spinal MRI disclosed C2–7 cord swelling. She also developed bilateral hilar lymphadenopathy, ocular uveitis, and an increased serum concentration of angiotensin converting enzyme (ACE). Endoscopic lymph node biopsy showed non-caseating epithelioid granuloma. These findings and the clinical features confirmed the diagnosis of spinal cord sarcoidosis. She underwent steroid pulse therapy (1000 mg/day of intravenous methylprednisolone over 3 succeeding days) and started taking oral prednisolone (60 mg/day) with benefit. Steroids were tapered to 40 mg every other day and 4 months later she was referred to our hospital. However, her gait difficulty relapsed together with urinary urge incontinence and voiding difficulty. She had constipation but no orthostatic hypotension. On admission to our hospital, she had spastic tetraparesis, which was dominant in the legs. Deep tendon reflexes were brisk with positive Babinski's signs. Sensations for pin prick and proprioception were decreased bilaterally below the C6 dermatome. Routine laboratory data were normal. Examination of CSF showed normal cell count (lymphocyte 1/mm^3) but mildly increased protein content (42 mg/dl). The ACE concentration was normal both in the serum and CSF. Spinal MRI disclosed C2–7 cord swelling which appeared as low signal intensity on T1 weighted images and high signal intensity on T2 weighted images (fig 1). Gadolinium-DTPA images showed contrast enhancement in the C4/5 intramedullary region which extended longitudinally through the surface of the spinal cord. She again underwent three courses of steroid pulse therapy and started taking oral prednisolone (40 mg/day) and cyclosporin (200 mg/day), which gradually ameliorated her neurological symptoms.

However, she began to have a sudden onset of severe, throbbing headache twice a week, which was accompanied by conjunctival congestion, facial flushing, lacrimation, and congestion of the nose, without evidence of skeletal muscle spasms or bowel contraction. Just before the attacks she felt only slight bladder sensation. Measurement of the blood pressure showed an extreme hypertension (190/100 mm Hg) without increasing heart rate (60 beats/min), although it showed a normal value between these attacks. On the first attack emergent brain CT disclosed no subarachnoid hemorrhage and 5 mg of sublingual nifedipine was applied. Autonomic dysreflexia was suspected and the bladder was catheterised, which showed a urine volume of 650 ml. These treatments ameliorated all of her symptoms and the hypertension within 30 minutes. We performed urodynamic studies, which showed voluntary voided volume of 79 ml with low maximum and average flow rates.[2] She had a postvoid residual volume of 350 ml (normal<30 ml). On EMG-cystometry, the first sensation was 350 ml (normal 100 ml−300 ml) and the maximum bladder capacity was

Table 1 IFN-γ allele and carriership frequencies in patients with Parkinson's disease (PD) and in healthy controls as well as in patient subgroups whose ages of onset are early (<50 y) and late (≥50 y)

	PD n (%)	Control n (%)	Early onset PD n (%)	Late onset PD n (%)
Allele (bp):				
116	1 (0.3)		1 (1)	
118	2 (0.6)	1 (0.3)		2 (0.8)
120	52 (15.3)	41 (13.1)	23 (23)	29 (12.1)
122	157 (46.2)	143 (45.5)	35 (35)	122 (50.8)
124	19 (5.6)	16 (5.1)	8 (8)	11 (4.6)
126	93 (27.4)	92 (29.3)	28 (28)	65 (27.1)
128	9 (2.6)	8 (2.5)	1 (1)	8 (3.3)
130	1 (0.3)	1 (0.3)	1 (1)	
132	6 (1.8)	12 (3.8)	3 (3)	3 (1.3)
Total	340	314	100	240
Carriership:				
122 carrier	117 (68.8)	109 (69.4)	28 (56)	89 (74.2)
122 non-carrier	53 (31.2)	48 (30.6)	22 (44)	31 (25.8)
Total	170	157	50	120

For combined alleles 116, 118, 130, and 132, allele frequency: early onset PD *v* late onset PD χ^2=14.3, df=5, Pc=0.028.
Carriership frequency: early onset PD *v* late onset PD χ^2=4.62, df=1, Pc=0.039.