The spinocerebellar ataxia type 1 expansions were found in three patients and dentatorubral-pallidoluysian atrophy expansions were found in five. The remaining six patients showed no expansion in any locus. After exclusion of these three types, three patients from two families having pure cerebellar ataxia with retained deep tendon reflexes and slight to moderate atrophy limited to the cerebellum on MRI, were diagnosed with ADCA type III. The remaining three patients from two families were suspected as having spinocerebellar ataxia type 2 because of decreased deep tendon reflexes, slow eye movement without nystugnus and pronounced atrophy in the pons and cerebellum on MRI.

In the nationwide epidemiological study in Japan without genetical evaluation reported by Hirayama *et al*,[5] Machado-Joseph disease occupied only 11% of all ADCA and was regarded as a relatively rare disorder. On the other hand, the Menzel type of hereditary cerebellar ataxia was 49% of all ADCA. Our findings, however, showed that Machado-Joseph disease, which accounted for 56%, is a common ADCA using the genetic estimation. Although the sample size of our study was not large enough to obtain good epidemiological reliability, a significant difference was shown by z test between the results of Hirayama *et al*[5] and our findings on Machado-Joseph disease ($P < 0{\cdot}002$) and on Menzel type of hereditary cerebellar ataxia ($P < 0{\cdot}002$), but not on dentatorubral-pallidoluysian atrophy. These differences may be due to the difficulty in clinical diagnosis of Machado-Joseph disease and Menzel type of hereditary cerebellar ataxia. In fact, five patients confirmed as having Machado-Joseph disease in this study were clinically suspected of having a Menzel type of hereditary cerebellar ataxia before the genetic analysis.

In conclusion, Machado-Joseph disease is a common ADCA in the Japanese and epidemiological re-examination of Japanese ADCA is necessary to obtain correct proportions of each genetically diagnosed disorder.

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Amyotrophic lateral sclerosis after accidental injection of mercury

Mercury has been widely discussed in the pathogenesis of amyotrophic lateral sclerosis.[1 2] We describe a case of amyotrophic lateral sclerosis after accidental injection of mercury.

While shaking a mercury thermometer, a female nurse plunged it into her left hand. Elementary mercury infiltrated into the soft tissues of her palm (figure). The diffusely distributed mercury particles could not be removed completely by surgical means. Two years later, blood mercury concentrations, analysed with atomic absorption spectroscopy, were raised (15 µg/l, reference < 5 µg/l), but declined soon afterwards to normal values.

Three and a half years after mercury infiltration, the 38 year old woman was admitted with progressive weakness of the legs which had begun a few weeks before. She had moderate weakness of the musculature—most pronounced in the lower limbs—slight cerebellar ataxia, and fasciculations in the thighs. Deep tendon reflexes were hyperactive at all her limbs. Babinski's sign was positive on the left. Cranial nerves and sensation were normal. Electromyography showed pathological spontaneous activity in muscles of both legs. Gastrocnemius muscle biopsy suggested neurogenic muscle atrophy. Mercury and lead concentrations in blood, urine, and hair were not raised. Medical history was unremarkable.

With a presumptive diagnosis of amyotrophic lateral sclerosis, we performed a chelation treatment with dimercaptosuccinic acid. Urinary mercury excretion increased (peak value 41·6 µg/24h, reference < 10 µg/24h) without clinical improvement. Muscular atrophy, cramps, and fasciculations become prominent in all limbs. Six months later, a severe bulbar syndrome developed.

Four years after the onset of neurological symptoms, the patient is tetraplegic. Communication is possible via eye movements. There is no respiratory insufficiency, sensory deficits, or dementia.

Mercury accumulates within the CNS, entering either by crossing the blood-brain barrier or via retrograde axonal transport. In our patient, mercury from the deposit in the hand could have slowly accumulated in the CNS over time. This would explain the dissociation between exposure to mercury and onset of clinical symptoms. Initial trauma and repeated surgical interventions may have enabled retrograde axonal transport.

It has been speculated that a pre-existing impairment or a genetically determined dysfunction of motor neuron metabolism could be aggravated by various exogenous factors such as trauma, triggering the manifestation of amyotrophic lateral sclerosis.[3] Thus mercury and trauma could have worked as synergistic factors in our patient.

Chelation treatment, as in this patient, has never been successful in amyotrophic lateral sclerosis. Such treatment—to be of any use—should be initiated shortly after exposure to mercury to prevent an accumulation and irreversible damage within the CNS.

Pure coincidence of a rare disease with an extraordinary preceding event cannot be ruled out, but the unusual appearance of amyotrophic lateral sclerosis in a young woman supports the role of mercury as a causative factor in this case.

In previous reports of motor neuron diseases after mercury incorporation, clinical symptoms developed shortly after the intake of large amounts of mercury and included typical signs of mercury intoxication.[1 2 4 5] Our patient illustrates the possibility that, if present over a longer period of time, relatively small amounts of mercury may cause sporadic amyotrophic lateral sclerosis without other signs of mercury intoxication.

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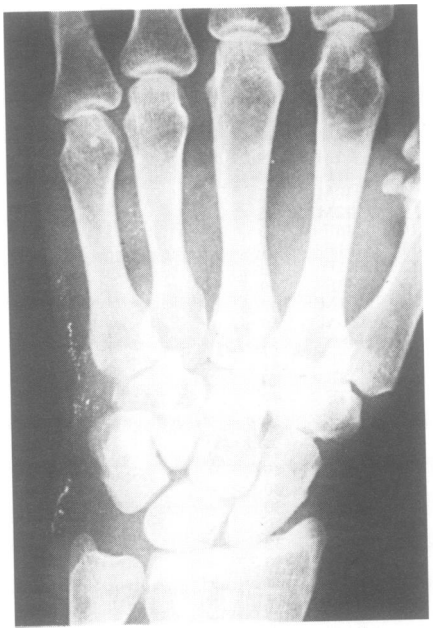

Radiograph of the left hand after injury with a mercury thermometer. Incorporated mercury particles are diffusely distributed in the soft tissues of the palm.