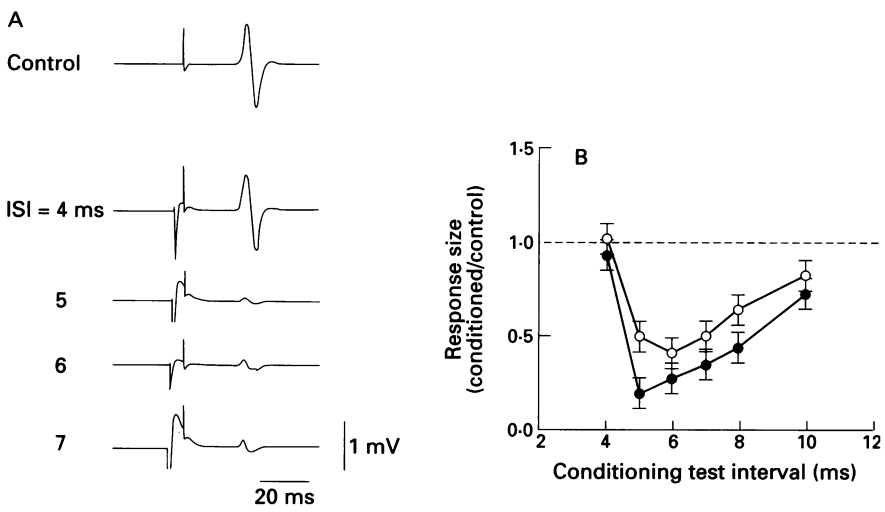

(A) typical responses in a patient with Fisher's syndrome. The first trace shows that the test magnetic stimulus over the motor cortex elicits a response of about 1·6 mV in peak to peak amplitude in the relaxed first dorsal interosseous muscle. Responses to the test stimulus given 4,5,6, and 7 ms after a conditioning electrical stimulus over the cerebellum are shown in the lower four traces. The conditioning stimulus has no effect on the response size when given 4 ms before the test shock. Responses are significantly smaller than the control response at interstimulus intervals of 5,6, and 7 ms. (B) Average (SEM) time course of suppressive effect on the motor cortex in the patients (closed circles) and normal subjects (open circles). The conditioned responses are significantly diminished at conditioning test intervals of 5,6, and 7 ms ($p < 0·01$) in both normal controls and patients. The two time courses are not significantly different ($p > 0·5$, ANOVA).

responses by unpaired Student's *t* test. The time course of the effect was made from the data of several blocks of trials. The average time courses for all the patients were compared with the normal values described elsewhere[2] by analysis of variance (ANOVA).

Traces in the figure (A) are typical responses in a patient with Fisher's syndrome. The test magnetic stimulus elicited a response of above 1·6 mV in peak to peak amplitude (first trace). The conditioning electrical stimuli significantly ($p < 0·01$) reduced the size of EMG responses to the test shock at interstimulus intervals of 5,6, and 7 ms (third to fifth traces). The size was not significantly ($p > 0·05$) affected by the conditioning stimuli when they were given 4 ms beforehand (second trace).

The figure (B) shows the average time course of suppression for all the patients with the average time course for normal controls. There were no significant differences between the two ($p > 0·05$, ANOVA).

Clinical features of our patients were all typical of Fisher's syndrome. Electrical stimuli over the cerebellum evoked a normal amount of suppression of motor cortical excitability in all patients. A comparison of these results with previous results obtained from patients with ataxia due to various disorders,[2 3] suggests that the efferent pathway from the cerebellar cortex to cerebellar nuclei, thalamus, and cerebral cortex is intact in patients with Fisher's syndrome. We conclude that ataxia in these patients is due either to an abnormality of the sensory afferent input to the cerebellum, or to abnormal processing of this input within the cerebellum.

Our conclusion is consistent with previous postulates that ataxia in Fisher's syndrome is due to dysfunction of the peripheral nervous system.[4] If some special components of proprioceptive sensation are disturbed, ataxia is a kind of sensory ataxia in our pathophysiological classification. Some other authors concluded that the main lesion was in the brainstem in Fisher's syndrome.[5] If this is the case, ataxia is produced by damage to the afferent systems to the cerebellum.

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Primary Sjögren's syndrome in chronic polyneuropathy presenting in middle or old age

Notermans *et al*[1] studied chronic idiopathic polyneuropathy presenting in middle or old age. In their routine evaluation, these authors looked for xerophthalmia and xerostomia, and serological tests for primary Sjögren's syndrome, without systematically performing a biopsy of the minor salivary glands. As some authors postulated that the classic clinical and laboratory features of primary Sjögren's syndrome may be absent,[2] we decided, three years ago, to investigate systematically, by biopsy of the minor salivary glands, patients with chronic idiopathic axonal polyneuropathy, when the results of extensive evaluation and follow up of six months were negative.

From 1990 to 1993, we performed biopsy of the minor salivary glands in 32 patients with chronic idiopathic axonal polyneuropathy, and found in seven cases an infiltration of the salivary glands by lymphocytes and plasma cells, and glandular destruction sufficient to reach grade 3 or 4 of Chisholm's classification. There were six women and one man, aged 56 to 80 (mean 65·8). The symptoms of the peripheral neuropathy appeared between the age of 50 to 70, except in one case. The manifestations of the sicca complex were often absent: two patients had a normal Schirmer's test, three had an increased sedimentation rate, and only one patient had a positive rheumatoid factor or antinuclear antibody test. Anti-Ro/SS-A and anti-La/SS-B antibodies were never present at significant serum titres.

The peripheral neuropathy was a purely sensory polyneuropathy in three cases, a sensorimotor polyneuropathy in two, and a mononeuropathy multiplex in two. Electrophysiological studies disclosed an axonal pattern in all cases. Nerve and muscle biopsies, performed in all cases, showed perivascular infiltrates by mononuclear cells in the muscle in one case, but necrotising vasculitis was never seen. A teased nerve fibres study confirmed predominant axonal degeneration in all cases. The course was usually slowly progressive and no patient was severely disabled. Four patients were treated with either steroids or plasma exchanges without clear improvement of the peripheral neuropathy.

There is no rule to date for performing a biopsy of the minor salivary glands in patients with chronic polyneuropathy of unknown cause, despite extensive evaluation. Primary Sjögren's syndrome is known to primarily affect middle aged women.[2 3] Predominantly sensory polyneuropathies seem to be more frequent than mononeuropathy multiplex.[3] Sensory neuropathies have been reported by other authors,[4] but seem to be rare. In addition, cerebral involvement, perhaps asymptomatic, may be present in some cases.[5] Griffin *et al* recommended biopsy of the minor salivary glands when Schirmer's test is considered positive. For most authors, two of the classic features (keratoconjunctivitis, xerostomia, and arthritis) are required to establish the diagnosis of primary Sjögren's syndrome,[3] but extraglandular involvement may overshadow the sicca syndrome or occur in the absence of glandular dysfunction.[2] On the other hand, biopsy of the minor salivary glands is a simple outpatient procedure that may provide an accurate diagnosis, even in the absence of clinical evidence of primary Sjögren's syndrome. We did not find side effects of this procedure in our series.

In conclusion, we suggest that appropriate evaluation of patients with chronic

axonal polyneuropathy should include biopsy of the minor salivary glands, even when there are few arguments in favour of the diagnosis of primary Sjögren's syndrome.

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Reliability of clinical diagnosis of Huntington's disease

Huntington's disease has a prevalence of between four and 10 per 100 000 in the United Kingdom.[1] It has severe and progressive physical and psychiatric effects. Onset symptoms are reported to be neurological in 46% of cases, psychiatric in 36%, and combined neurological and psychiatric in the remainder.[2] There is thus considerable potential for misdiagnosis.

The cloning of the gene responsible for Huntington's disease showed that the disorder is caused by an expansion of a CAG trinucleotide repeat in the 5' transcribed region. The original report[3] suggested that normal people had 11 to 34 copies of the repeat and those affected with Huntington's disease had 42 to 100 copies. Our own studies with an improved polymerase chain reaction assay that measures only the specific size of the CAG repeat[4] show that the copy number in normal subjects extends from 8 to 33, whereas the lower end of the Huntington's disease range starts at 35.[5]

As we find no overlap between the two distributions, it is possible to use CAG measurement to estimate how often Huntington's disease is clinically misclassified. We have already reported three incorrect diagnoses in a series of 340 with purported Huntington's disease (0·9%), made up of one with presenile dementia of the Alzheimer type, one with multi-infarct dementia, and one with Parkinson's disease.[5] We have now searched for missed Huntington's disease diagnoses in a series of 221 patients with diagnoses of schizophrenia, 79 with presenile dementia of the Alzheimer type, and 68 with senile dementia.

The figure shows the distributions of CAG repeats. There were two possible missed cases of Huntington's disease in the set of 368 patients with psychiatric disorders. One patient, who died at age 88 after a stay in hospital of 42 years and a diagnosis of schizophrenia, had a CAG repeat size of 36. There was no family history of Huntington's disease. At necropsy the brain was removed and fixed intact for a complete neuropathological study. Findings were consistent with a diagnosis of schizophrenia and no abnormality was detected in the caudate. The second patient, who died at age 68 of presenile dementia of the Alzheimer type, had a CAG repeat size of 34. There were no extrapyramidal signs of Huntington's disease at necropsy. Re-examination of the case notes and a further report from medical and nursing staff caring for the patient suggested no symptoms of Huntington's disease.

In all other respects the CAG distributions among the psychiatric disorders were identical to the distribution among normal subjects. There is currently debate about the existence and extent of possible overlap between the normal and Huntington's disease CAG repeat sizes. Although this is yet to be resolved, our finding of a maximum of two missed cases of Huntington's disease (if that is what they were) in 368 patients with psychiatric disorders should increase confidence in the new molecular assay.

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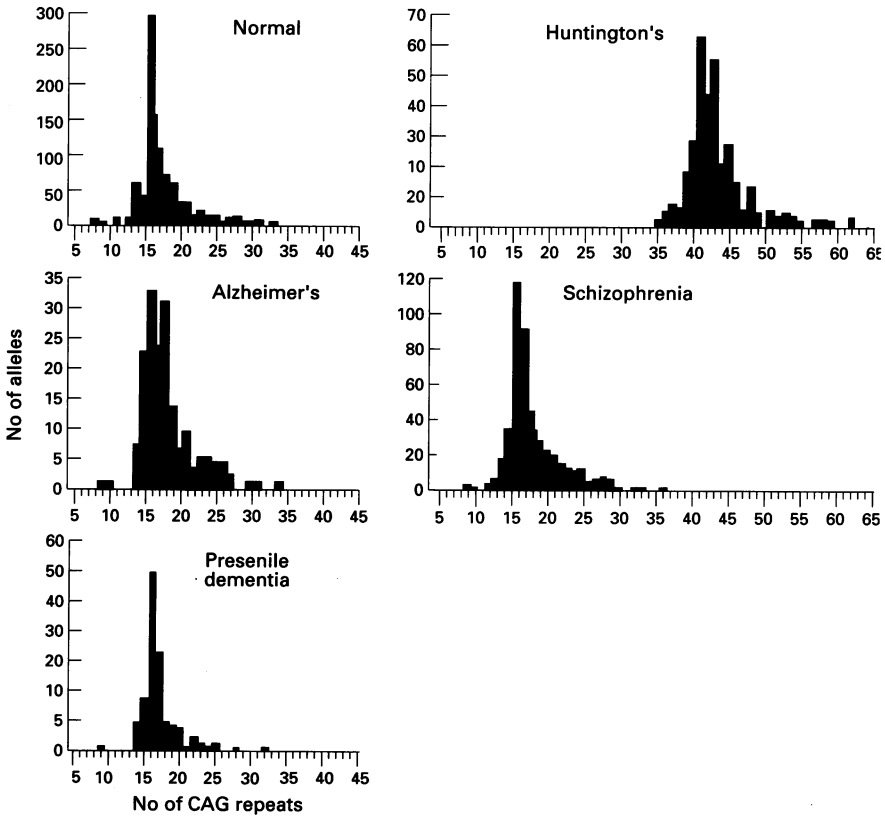

Distribution of CAG repeats in normal subjects and patients with various psychiatric disorders.

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Effect of sudden episodic intracranial hypertension on the electroencephalogram in a child with head injury

There is some controversy regarding the treatment of raised intracranial pressure, particularly in the very young, where the upper limit of normal intracranial pressure is below 5 mm Hg.[1] There is a general consensus that active treatment should be instituted for sustained intracranial pressure of 25 mm Hg or greater in adults. Intervention in children, however, needs to take account of the lower values of intracranial pressure, blood pressure, and cerebral perfusion pressure, and there are limited data for critical thresholds in children. Ideally treatment should be based on multimodality monitoring of cerebral blood flow and metabolic function.[1] This case report shows the functional consequence on brain electrical activity of acute intracranial hypertension and concomitant changes in cerebral perfusion pressure in a young child with head injury.

An 18 month old male child sustained a severe, coma producing, non-accidental