

SHORT REPORT

Chronic inflammatory demyelinating polyradiculoneuropathy: a prevalence study in south east England

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Abstract

Although there are now widely accepted diagnostic criteria for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) there are few epidemiological data. A prevalence study was performed in the four Thames health regions, population 14 049 850. The prevalence date was 1 January 1995. Data were from a national consultant neurologist surveillance programme and the personal case series of two investigators. A diagnosis of CIDP was made according to definite, probable, possible, or suggestive diagnostic criteria. A wide difference in prevalence rates between the four health regions was noted, probably due to reporting bias. In the South East Thames Region, from which the data were most comprehensive the prevalence for definite and probable cases was 1.00/100 000; the highest total prevalence (if possible and suggestive cases were included) would have been 1.24/100 000. On the prevalence date 13% of patients required aid to walk and 54% were still receiving treatment.

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Forty years ago Austin reported 32 cases of "steroid responsive polyneuropathy".¹ In 1982, after many case series which illustrated the heterogeneity of the condition, Dyck *et al*² coined the term chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). In 1991 research criteria for diagnosis were published,³ to which refinements or alternatives have been proposed.⁴ Large recent case

series have documented the range of presentation, course, and treatment response of CIDP.⁵⁻⁸ However, there are few epidemiological data for CIDP and only two estimates of prevalence.^{9 10} We studied a population of more than 14 million people in south east England, to determine the minimum prevalence, age and sex distribution, and morbidity of CIDP.

Methods

GEOGRAPHY AND POPULATION BASE

Population statistics for the North West Thames (NWT), North East Thames (NET), South West Thames (SWT), and South East Thames (SET) Regional Health Authorities of England were obtained from the Office of Population Censuses and Surveys. The nearest population estimate to the prevalence date was that in mid-1993 when the total population for all Thames regions was 14 049 850, and of the South East Thames region 3 717 638.

DATA COLLECTION

From October 1994 until March 1995 cases of CIDP were sought through the British Neurological Surveillance Unit from neurologists serving the four Thames health regions. Details of cases were requested from the reporting neurologist by letter. Diagnostic and treatment data were obtained on a standardised form completed by the reporting neurologist, or by us directly from the patient's hospital notes. In addition, the personal series of cases resident in the Thames regions of two of the investigators (RACH and PKT) were included. The prevalence date was 1 January 1995.

Demographic, clinical, CSF, nerve conduction, and sural nerve biopsy data were collected. The modified Rankin scale¹¹ (table) was used to assess handicap as an indicator of

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*Modified Rankin scale*¹¹

Grade	Description
0	No symptoms
1	No significant disability despite symptoms: able to carry out all usual duties and activities
2	Slight disability: unable to carry out all usual duties but able to look after own affairs without assistance
3	Moderate disability: requiring some help, but able to walk without assistance
4	Moderately severe disability: unable to walk without assistance, and unable to attend to own bodily needs without assistance
5	Severe disability: bedridden, incontinent, and requiring constant nursing care and attention

morbidity both at the prevalence date and at the nadir of illness. Type of medical treatment was recorded, but not dosage, efficacy, or side effects.

The study had the approval of the ethics committee responsible for Guy's Hospital.

DIAGNOSTIC CRITERIA

Cases were classified according to the following diagnostic criteria based on those of the ad hoc subcommittee.³ Patients had to fulfil a clinical diagnosis of CIDP, with relapsing or progressive sensory and/or motor manifestations attributable to peripheral nerve dysfunction, present in more than one limb for at least 8 weeks with generalised hypoflexia or areflexia.³ A CSF examination had to fit the criteria of the ad hoc subcommittee (cell count <10 mm³, negative venereal disease research laboratory test). Patients were further subclassified into definite (established by biopsy); probable (fulfilling the clinical, CSF, and electrophysiological criteria of the ad hoc subcommittee, but with no, or a non-diagnostic, biopsy); possible (fulfilling clinical and CSF criteria of the ad hoc subcommittee and having been diagnosed by a consultant neurophysiologist as having an acquired demyelinating neuropathy); or suggestive (fulfilling the clinical criteria so that CIDP was the preferred clinical diagnosis but the other criteria were not fully met—for example, CSF not examined).

The clinical course of the illnesses was recorded and classified as monophasic, progressive, relapsing-remitting, or recurrent Guillain-Barré syndrome. Monophasic illness fulfilled the clinical criteria for CIDP and then remained stable or improved for at least 6 months. Progressive disease worsened steadily showing no improvement with or without treatment up to the time of observation. A relapsing course was defined as at least two episodes of rapid worsening, demonstrable symptomatically or through clinical examination and with or without treatment, lasting more than 7 days and following a period of stability or improvement of at least 4 weeks.

Sural nerve biopsies showing unequivocal evidence of segmental demyelination or remyelination and without features of other specific pathology were considered diagnostic. Cases with an associated paraprotein were excluded.

Results

Between October 1994 and March 1995, 28 cases were reported to the British Neurological Surveillance Unit and details of 13 of these cases were subsequently made available to the investigators by the reporting neurologist. Seven cases fulfilled the diagnostic criteria and six were alive at the prevalence date. Eighty eight cases were known to the investigators as part of their personal series. Ten other cases (four in the SET region) were identified but could not be contacted and these were excluded. In total, 94 cases were identified giving a minimum prevalence rate (all categories of diagnosis) of 0.67/100 000 population for

the whole of the four regions on 1 January 1995. There were marked regional differences in the numbers of patients reported and, as a result, in the prevalence rates from each of the four regions. These were: 0.51 (NWT), 0.47 (SWT), 0.46 (NET), and 1.24 (SET)/100 000 population.

Complete data were available for the 46 patients in the SET region. They were 26 males and 20 females with a mean age of 54.4 (SD 17.8) years (range 10–95). There was no significant difference in the ages of the male and female populations ($p=0.25$). The age of onset was 45.6 (SD 17.7) years. There were no significant differences in the ages of onset of disease in males or females. The age of onset of the relapsing-remitting subgroup was 41.8 (SD 18.3) years which was slightly, but not significantly, less than the monophasic/progressive subgroup (50.0 (SD 17.0) years). The disease duration at the prevalence date was 8.9 (SD 7.6) years (range 2–490 months). Six cases (13%) were monophasic, 20 (43%) relapsing-remitting, and 17 (37%) progressive. Three cases (7%) had varying, but often short, times to the nadir of their relapses and were classified as recurrent Guillain-Barré syndrome.¹² There were no cases of multifocal motor neuropathy with conduction block in the SET region, although two were identified in the other three regions.

All the patients in the SET region fulfilled the clinical diagnosis for CIDP. Forty five (98%) had a lumbar puncture, the results of which were available in 38 patients and these fitted the criteria of the ad hoc subcommittee.³ Electrophysiological examinations were available for 44 patients. In 70% of cases (32/44 of the examinations) the EMG fulfilled the criteria of the ad hoc subcommittee.³ In 26% (12/44) the examination was not able to fulfil the criteria set down for demyelination, but in five the consultant neurophysiologist performing the EMG confidently diagnosed a demyelinating neuropathy (sural nerve biopsy was performed in two of these and confirmed segmental demyelination and/or remyelination). Three studies did not fulfil the EMG criteria for demyelination (but in two of these three, biopsy showed demyelination and/or remyelination) and in four insufficient data were obtained to categorise the neuropathy (two were biopsied; one biopsy showed demyelination and/or remyelination and one did not). In 63% (29/46) of patients a nerve biopsy was available for examination and in 37% of patients (17/46) this provided histological confirmation of demyelination and/or remyelination. As a result of this information the diagnosis was considered definite in 17 (37%), probable in 20 (43%), possible in three (7%), and suggestive in six (13%) cases.

A minimum prevalence estimate in the SET region based on definite diagnostic criteria alone is therefore 0.46/100 000 population (95% confidence interval (95% CI) 0.27–0.73) and the figure for combined definite and probable cases (by the usual clinical criteria) is 1.00/100 000 (95% CI 0.70–1.37).

The average modified Rankin scale score at the nadir of the worst relapse was 3.5 (SD 1.1). Over half (54%) of the patients had scored grade 4 or 5 at some time during their illness. At the prevalence date the median modified Rankin scale score was 1.5 (SD 1.4) (range 0–5), and 13% were still dependent on others to walk and attend to their bodily needs (modified Rankin scale score 4–5).

Forty patients (87%) had received corticosteroids at some time in their illness, and at the prevalence date 20 were on continued treatment. Eleven (24%) had tried intravenous immunoglobulin and seven were still receiving courses of treatment at the study date. Fifteen had received plasma exchange and 21 azathioprine. Three had tried cyclosporin.

Ten (22%) patients were receiving more than one treatment at the prevalence date, all of these receiving prednisolone with intravenous immunoglobulin or plasma exchange or azathioprine as well. There was no significant difference in the modified Rankin scale score between the patients treated with one, or more than one, intervention at the prevalence date. Seventeen of 21 patients receiving no treatment at the prevalence date were in remission with no or minimal symptoms (modified Rankin scale score 0–1).

Discussion

We found a minimum population based prevalence for CIDP of 0.67/100 000 population (range 0.46–1.24/100 000). The prevalence obtained from one health region (SET) within that population for definite and probable CIDP (by the usual clinical criteria) was 1.00/100 000. The prevalence estimate for patients with definite (established by biopsy) CIDP only in the SET region was 0.46/100 000.

The tertiary referral centre serving the SET region has a special interest in inflammatory neuropathy, which might account for the greater case ascertainment than in other regions. We think that the estimated prevalence of 1.00/100 000 is likely to be a better estimate of minimum prevalence and it agrees with two previous population studies.^{9 10} Kusumi *et al*⁹ gave a prevalence of 0.81/100 000 (95% CI 0.26–1.90) based on five patients in a population of 614 725 people in a Japanese prefecture. Mohamed *et al*¹⁰ found a higher prevalence of about 1.95/100 000 in Newcastle, New South Wales (population about 1 million).

The demographic data of the patients in the SET region resemble those of large published studies including the male preponderance, the trend towards earlier onset of disease in the relapsing-remitting group than in the monophasic/progressive group, and the proportion of relapsing-remitting to progressive cases.^{5–7 13}

We excluded all cases that had an associated paraproteinaemia on the grounds that most form a separate group. In some cases the association of demyelinating neuropathy and paraprotein will be by chance alone. Cases associated with IgM antibody with reactivity to

myelin associated glycoprotein form a homogeneous group with distinguishing clinical features. Many others are likely to fall into such subgroups in the future. Only a small proportion of cases remain indistinguishable from CIDP¹⁴ apart from the presence of a paraprotein.

Two cases of multifocal motor neuropathy with conduction block (MMNCB) were identified and included. Clinical distinction of MMNCB from CIDP is not always easy as patients with MMNCB may have subtle sensory symptoms and signs, abnormal sensory nerve conduction studies, and inflammatory changes on sural nerve biopsy.¹⁵ The features of nerve conduction found in MMNCB fit within the ad hoc subcommittee criteria for CIDP used in this study. The approach to treatment of the two conditions differs; MMNCB does not respond to, and sometimes worsens, with steroids but it remains contentious as to whether MMNCB and CIDP are two manifestations of one disease, or two diseases.^{16 17}

This study provides the first estimate of the prevalence of disability from CIDP. Although we have no data on the duration of individual relapses, 54% had been unable to lead an independent existence at some stage during their illness and at the prevalence date this figure was 13%. The healthcare costs are likely to have been substantial.

Although this study provides the most accurate estimate of prevalence of CIDP yet available, we recognise its shortcomings. Future studies should collect data prospectively, with clearly defined but less rigid neurophysiological criteria than those proposed by the ad hoc subcommittee; use a longer surveillance period to increase reporting; include and compare cases with paraproteinaemia; and record more comprehensive data about treatment, response and complications, and disability.

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NEUROLOGICAL STAMP

Alexander Onufrievich Kovalevsky (1840-1901)

Alexander Kovalevsky was born on 7 November 1840 in Dvinsk in Russia, studied medicine at the University of Heidelberg, and was Professor of Embryology at the University of St Petersburg. He showed that all animals pass through the gastrulation stage (the process by which the young embryo acquires its three germ layers). Eponymously he is remembered by the neuroenteric canal of Kovalevsky, also known as the blastophoric canal in the embryo.

Kovalevsky was the Russian founder of comparative embryology and experimental histology. His demonstration of a common development pattern in the embryological development of multicellular animals, both vertebrates and invertebrates, provided important evidence of the evolution of living organisms. In 1890 he was elected to the Russian Academy of Sciences.

In 1951 Kovalevsky was portrayed on one of a series of stamps of Russian scientists. (Stanley Gibbons 1719, Scott 1569).

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