

Huntington disease in County Donegal: epidemiological trends over four decades.

P J Morrison N C Nevin

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SUMMARY

The prevalence rate of Huntington disease in County Donegal between 1961 and 1991 showed a decrease from 4.4 to 1.6 per 100,000 population. Emigration and reduction in family size probably account for the progressive decline in prevalence. Over the same time period in the rest of Europe, prevalence has declined only gradually, or has remained static.

INTRODUCTION

Huntington disease, due to an autosomal dominant gene, is characterised by cognitive dysfunction, psychiatric disturbance and movement disorder. (The term Huntington disease is now preferred to the possessive Huntington's disease). The gene has been localised on chromosome 4, and affected patients have a trinucleotide repeat expansion¹ of their IT15 gene². The prevalence of Huntington disease has been extensively studied in the United Kingdom (Table I), and is between 4 and 10 per 100,000³. In Northern Ireland the prevalence rate is 6.3 per 100,000^{4,5}. There is no prevalence data available for the Republic of Ireland. County Donegal was historically part of the province of Ulster, and, until the partition of Ireland, had closer population links with Northern Ireland than with the rest of Ireland^{6,7}. We have investigated Huntington disease in County Donegal with the aims of ascertaining all living and deceased individuals with the disease, of estimating trends in prevalence rates, and of establishing a genetic register of affected and 'at risk' individuals to ensure that long term support and advice is available to families.

METHODS

The index Huntington disease patients were identified using multiple sources of ascertainment. Early in 1992, a circular was sent to all general practitioners, neurologists and psychiatrists, in the Republic of Ireland, requesting the name and address of known Huntington disease patients, living or deceased. Further contacts with the regional neurologist, regional psychiatrists, and general practitioners in County Donegal were made in person or by telephone or letter. The diagnostic records in the Department of Medical Genetics at the Queen's University of Belfast, which date from 1967, were examined. These are the

Department of Medical Genetics, The Queen's University of Belfast, Belfast City Hospital, Belfast BT9 7AB.

P J Morrison, MD, Royal College of Physicians of Ireland Glaxo Fellow in Molecular Biology.

N C Nevin, MD, Professor of Medical Genetics

Correspondence to Dr Morrison.

clinical records of patients attending the genetic counselling clinics, including the satellite clinic in Altnagelvin hospital, County Londonderry, where patients from County Donegal may be seen. No genetic counselling service exists in the Republic of Ireland. In addition, from detailed examination of the pedigrees and by visiting affected patients and relatives in their homes, other affected and 'at risk' individuals were identified.

Estimates of prevalence rates per 100,000 population were made for 1961, 1971, 1981 and 1991, using the dates of the decennial census in Ireland. The prevalence rate was estimated using the formula

$$P = X/Y \times 100,000$$

where X = number of affected living Huntington disease patients,

and Y = the total population (obtained from the Central Statistics Office, Dublin).

TABLE I

Prevalence of Huntington disease per 100,000 population in County Donegal.

Year	Affected	Population	Prevalence
1926	7*	152508	4.6
1961	5	113842	4.4
1971	3	108344	2.8
1981	2	125112	2.0
1991	2	128117	1.6

* this older figure is most likely an underascertainment

RESULTS

All families ascertained have been domiciled in County Donegal for many decades. No patients were ascertained who had recently emigrated from other parts of Ireland or from the United Kingdom. The prevalence rates are shown in Table I. Reliable estimates are not available prior to 1955, but for comparison, a minimum historical estimate is shown for 1926. Twelve cases were identified over the period 1961-1991. One patient is still alive. For all patients, the mean age at onset was 40.7 years with a mean age of diagnosis of 44.4 years. For the 11 deceased patients, the mean age at death was 49.8 years. The mean duration of the disease was 12.3 years.

DISCUSSION

The survey is virtually a total ascertainment of Huntington disease patients in County Donegal. This was achieved because the area covered is small, personal contact with medical practitioners was feasible, and thorough primary and secondary family tracing was possible. Categories of Huntington disease patients liable to under-ascertainment in larger population studies such as new mutations, families with no current affected living members, or affected individuals from outside the area, are unlikely to have been excluded from this study.

All the patients appear to have a familial origin in County Donegal for at least five decades, and indeed some families can be traced back to the early 1800's. The prevalence rate has steadily declined as 'at risk' siblings and children have emigrated to other parts of Ireland, the United Kingdom or abroad. Several affected emigrant members have been traced to the United Kingdom⁴. County Donegal is mainly a farming community with no major industries. Over the last five decades, the population has decreased, mainly due to emigration of employable members of the population seeking employment outside the county. The birth rate also has decreased as younger people move away. The ages of onset and diagnosis are similar to other published studies^{3,4}. The age of death is slightly lower. Only one patient with juvenile Huntington disease has been identified, with an age of onset of 10 years, diagnosis at 14 years, and death at 21 years. Only one patient had an onset over 50 years of age.

TABLE II
Huntington disease: minimum prevalence per 100,000 population in the British Isles

Area	Reference *	Year	Prevalence
<i>ENGLAND:</i>			
Home Counties	Critchley	1934	0.2 - 1.3
London	Minski, Guttman	1938	1.8
Cornwall	Bickford, Ellison	1953	5.6
Northamptonshire	Pleydell	1954	4.9
Northamptonshire	Pleydell	1955	6.0
Northamptonshire	Reid	1960	7.2
Northamptonshire	Oliver	1970	6.3
Carlisle (Cumberland)	Brewis	1966	2.8
N E London/Essex	Heathfield	1967	2.5
Bedfordshire	Heathfield, Mackenzie	1971	7.5
Somerset	Glendenning	1975	5.5
Leeds/Yorkshire	Stevens	1976	4.2
East Anglia	Caro	1977	9.2
<i>SCOTLAND:</i>			
Moray Firth	Lyon	1962	560.0
West Scotland	Bolt	1970	5.2
Edinburgh & Lothian	Venters	1970	6.5
Grampian	Simpson, Johnston	1989	9.9
<i>WALES:</i>			
South Wales	Harper	1979	7.5
South Wales	Walker	1981	7.6
South Wales	Quarrell	1988	8.5
North Wales	Quarrell	1988	5.5
<i>IRELAND:</i>			
Northern Ireland	Morrison	1991	6.3
Republic of Ireland (County Donegal)	Present study	1991	1.6

* These studies can be found in detail in references 3, 4, 5, 8, 9.

The trend for the Huntington disease prevalence rate to decline is likely to continue. In 1993, only one patient with the disease was living in County Donegal, and few 'at risk' patients remain. Population studies in Wales⁸ over a 30 year period show a gradual downward trend in the prevalence of Huntington disease. The downward trend in our survey has been more rapid due to emigration of 'at risk' patients, and a reduction in size of the families compared to previous generations.

This study, involving a small area, illustrates how random genetic drift in more isolated populations has a more extreme effect on the prevalence of the disease than in a larger population area. The very high concentration of Huntington disease in the Moray Firth area in Scotland⁹ shows the opposite effect, with genetic isolation causing a very high prevalence rate, (Table II).

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