

A genetic disease

Huntington's disease (HD) was first described in 1872 by Dr George Huntington after whom it is named.¹ It is a genetic disease causing persistent neurodegeneration, manifesting in movement, cognitive and psychiatric disturbances that progress over a 10-20 year period, inexorably towards death. The HD gene was identified in 1993² and children of a parent with HD have a 50/50 chance of inheriting the disease. The prevalence of HD is 1 in 10,000, with approximately 6,000 HD patients in the UK.

There are currently no treatments that alter the progression of the disease. Physicians treat the symptoms they can with the medicines available to them. However, there is limited research, and even less consensus as to the optimum treatment regime. Furthermore, commonly prescribed treatments can result in the worsening of other symptoms, or can introduce new side effects. It is incredibly disappointing to note that the survival of HD patients in regions where medical technology is largely unavailable is similar to that of populations with ready access to treatment.^{3,4} New treatments are urgently required, as is robust clinical testing of the currently prescribed therapies to agree on an optimal treatment regime.

There are currently just nine compounds in clinical trials as treatments for HD.³ HD is an 'orphan disease' as it affects a relatively small percentage of the population. The European Union and the US, as well as Japan and Australia, have recognised that there are barriers to developing new drug therapies for orphan diseases and have introduced

regulations offering marketing incentives and fee reductions in order to try and increase the number of drugs being developed. Despite this, the number of clinical trials in HD remains depressingly low.

Developing new treatments for any disease or disorder is a challenging business and this is even greater in the case of HD. Finding sites with sufficient numbers of patients can be an issue: patients are scattered throughout the country and in the UK there are few central specialist centres, with no standard referral system, so very often patients will be treated by a doctor with only a limited understanding of the disease. Consequently, prescribing practices vary widely, and this can cause difficulties if the clinical trial design desires a setting limiting usage of concomitant medication. Although the test used to measure the progression of HD, the Unified Huntington's Disease Rating Scale (UHDRS)⁵, is well established and has been used in a number of clinical trials, it has limitations as a useful tool for drug developers⁶. It is particularly limited in clinical trials of a short duration (ie. less than six months). The longer it takes to run a clinical trial the more expensive that trial becomes. What is required is an improved, validated and clinically relevant scale, or scales, to measure the disease.

As well as improved measurements of the disease, everyone would benefit from the creation of specialist treatment centres for HD in the UK, where patients could be treated by a clinician that is an expert in the field. In countries such as the US and Canada, it is routine that HD patients are automatically referred on to a

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specialised centre, so-called 'Centres of Excellence', which see many hundreds of HD patients. Finally, each centre could adopt a standard protocol of care and a properly researched and tested treatment regime.

QCTR is a CRO specialising in CNS disorders. We are particularly experienced in designing and conducting clinical trials in HD and have extensive experience in dealing with US and EU regulators on developing new therapies as treatments for HD.

- ¹ Huntington G, On chorea. *George Huntington MD, J Neuropsychiatry Clin Neurosci*, 2003, 15: 109-12
- ² The Huntington's Disease Collaborative Research Group, A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. *Cell*, 1993, 72: 971-83
- ³ Walker FO, Huntington's disease. *Lancet*, 2007, 369: 218-28
- ⁴ Craufurd D and Snowden J, Neuropsychological and neuropsychiatric aspects of Huntington's disease. In: Bates G, Harper P, Jones L, eds. *Huntington's disease*. New York: Oxford University Press, 2002: 62-94
- ⁵ Huntington Study Group, Unified Huntington's disease rating scale: reliability and consistency. *Movement Disorders*, 1996, 11: 136-42
- ⁶ Mahant N et al, Huntington's disease: clinical correlates of disability and progression. *Neurology*, 2003, 61: 1085-92



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