

GEORGE HUNTINGTON'S "ON CHOREA" AFTER 150 YEARS: HOW A "FEW WORDS" CHANGED THE HISTORY OF A DISEASE

Castillo-Torres Sergio A. ^{1,2} 

1. Servicio de Movimientos Anormales, Departamento de Neurología, Fleni. Buenos Aires, Argentina.
2. Servicio de Neurología, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León. Monterrey, NL, México.

Correspondence

Sergio Andrés Castillo Torres
Servicio de Movimientos Anormales
Departamento de Neurología, Fleni
Montañeses 2325, Capital Federal,
C1428AQQ, Buenos Aires, Argentina.

[✉ sact.md@gmail.com](mailto:sact.md@gmail.com)

Source of financing: none.

Declaration of conflicts of interest

Dr. Castillo-Torres serves as Senior Editor in Neurology, and Section Editor (Neuroscience, History and Philosophy) for Archivos de Neurociencias.

Author Contributions

Dr. Castillo-Torres: Conception and design, drafting, final approval, agreement to be accountable.

Acknowledgments: none.

"In the whole range of descriptive nosology there is not, to my knowledge, an instance in which a disease has been so accurately and fully delineated in so few words were given."

Sir William Osler, *On Chorea and Choreiform Affections* (1894)

Huntington's disease (HD, OMIM #143100) is an autosomal dominant neurodegenerative disorder caused by a repeat expansion of the CAG trinucleotide in the Huntingtin gene (Htt), located on chromosome 4 (4p16.3). Clinically, it is widely known for chorea: an involuntary hyperkinetic movement disorder characterized by movements apparently flowing from one body part to another in a random, non-rhythmic, and non-patterned fashion.¹

The term "chorea" comes from the Greek χορεία (khoreía), meaning "a round dance". It was first proposed by Paracelsus in the XVI century to describe the main symptom of St. Vitus' dance, also known as the dancing disease;² which he suggested to rename *chorea lasciva* (unrestrained dance), attributing it to the sufferer's imagination, since neither "God or the Saint inflict it". In contrast, *chorea naturalis*, or of natural ("organic") origin, was considered to require medicines to be treated.²

Before Paracelsus' treatise, interest in chorea as a disorder appears to be scarce, with few reports on the subject until the early seventeenth century, when only a handful of German and English physicians wrote about it. Among them, the most remarkable is Thomas Sydenham, who in 1686 described the infantile form of chorea, which is known by his name, even though he initially confused it with a religious procession and called it *Chorea Sancti Viti*. William Osler later reclassified Sydenham's chorea as *chorea minor*, reserving the term *Chorea Sancti Viti* dance for the religious dance.³

Although adult chorea is now almost synonymous with Huntington's disease (HD), there is scant historical evidence of hereditary chorea cases prior to George Huntington's observations in the 19th century. This can be attributed to several factors.



Firstly, the fact that adult-onset or hereditary cases were considered infrequent or even non-existent. Additionally, the lower life expectancy during and prior to the 19th century meant that patients with hereditary chorea died before they could manifest choreic symptoms or have descendants who carried the disease.⁴ Furthermore, prevailing beliefs that hereditary chorea was a curse might have prevented afflicted families from openly discussing the matter.

George Huntington published "On chorea" on April 13th, 1872, in *The Medical and Surgical Reporter*.⁵ His article commenced emphasizing the essential features of chorea: motor impersistence ("tongue is protruded and suddenly withdrawn") and the haphazard nature of the movements ("The contortions are never localized to one muscle or set of muscles, but the whole muscular system seems to be involved").⁵ Huntington then proceeded with a review of the post-infectious form of chorea (Sydenham's chorea), and its association with rheumatism, highlighting the importance of cardiac examination.⁵ Afterwards, he criticized the limited evidence concerning the underlying pathological changes in patients with chorea, hoping one day these would be "laid open to the light of day".⁵ The article concluded with a brief review of the therapeutic agents used during that era, ranging from purgatives to electricity, each with varying degrees of success.⁵

After this general perspective of chorea, Huntington presented the case for *hereditary chorea*. Although at the time of writing he was 22 years old and had been licensed as a physician for only one year, the conception of the article had been lingering in his mind for nearly 14 years. Huntington traced his interest in *hereditary chorea* back to the beginning of his medical education, at the age of 8, while accompanying his father on his rounds and witnessing a mother and daughter afflicted with "that disorder", as it was usually referred to in families.^{6,7} Thus, his observations also relied upon the experience of his father and grandfather, who were also physicians and had registered cases of *hereditary chorea* since the early eighteenth century.^{7,8}

Huntington underscored three characteristics of the disease: 1) its hereditary nature; 2) a predisposition towards cognitive decline and suicide; and 3) the manifestation of severe disease only in adults, with no reported cases occurring before the age of 30.⁵ Of these, only the third feature did not withstand the test of time, since today we know that young adults and even children can manifest HD from an early age, particularly as a rigid-akinetic syndrome known as the Westphal variant.

Huntington concluded his article by declaring that he considered *hereditary chorea* "merely as a medical curiosity". Unknowingly, his work would help to bring attention to a disease that had remained ignored by the medical community. Less than a decade after this publication, *hereditary chorea* was renamed as "Huntington's chorea" (Browning, 1908, as cited by Lanska).⁷

Nonetheless, this eponym was not universally accepted, and figures like Jean-Martin Charcot argued against it, proposing that *hereditary chorea* had its origins in infantile chorea.⁹ However, other prominent figures in the medical field, such as William Osler and William Gowers, advocated for its acceptance, recognizing the value of Huntington's observations.¹⁰ Despite the existence of at least three reports on *hereditary chorea* prior to Huntington's work (thoroughly analyzed by Lanska),⁷ these did not receive widespread attention. However, they were acknowledged by Huntington himself shortly after his report gained recognition from the medical community, redirecting their attention to the subject of *hereditary chorea*.

Huntington's report provides a noteworthy example of the power of observation and its relevance as an indispensable quality for practicing neurologists.¹¹ Much like James Parkinson's essay on the shaking palsy, neither Huntington's report nor the earlier ones included detailed information about specific patients.¹² As stated by the opening quote from Sir William Osler, the history of a disease can be altered with only a "few words". Thus, reminding us that meticulous clinical observation and precise description of findings remain relevant, even in the presence of advanced medical technologies.

In 1984, British neurologist McDonald Critchley reviewed the history of Huntington's chorea and expressed concern over the absence of "clinical, anthropomorphic, electroencephalographic, biochemical, or pharmacological" markers to recognize premanifest HD carriers.¹³ Nevertheless, in the 150 years that have past since George Huntington's seminal description, most of these features have been "laid open to the light of day",⁵ allowing for the detection of premanifest carriers and facilitating research on potential disease-modifying therapies. Contrary to Critchley's opinion that "the end is not yet in sight",¹³ we are now closer than ever to witnessing the beginning of the end of HD.

References

1. Marsden CD, Donaldson I. Marsden's book of movement disorders. Oxford: Oxford University Press; 2012.

2. Temkin CL, Rosen G, Zilboorg G, Sigerist HE. Four Treatises of Theophrastus Von Hohenheim called Paracelsus. Baltimore: The Johns Hopkins Press; 1941.
3. Osler W. On chorea and choreiform affections. London: H. K. Lewis; 1894.
4. Stevens DL. The history of Huntington's chorea. J R Coll Physicians Lond. 1972;6(3):271-82.
5. Huntington G. On Chorea. Medical and Surgical Reporter. 1872;26:320-1.
6. Lanska DJ. Chapter 33: the history of movement disorders. Handb Clin Neurol. 2010;95:501-46. doi: [10.1016/S0072-9752\(08\)02133-7](https://doi.org/10.1016/S0072-9752(08)02133-7)
7. Lanska DJ. George Huntington (1850-1916) and hereditary chorea. J Hist Neurosci. 2000;9(1):76-89. doi: [10.1076/0964-704X\(200004\)9:1;1-2;FT076](https://doi.org/10.1076/0964-704X(200004)9:1;1-2;FT076)
8. Wexler A. A brief prehistory of Huntington's disease. J Huntingtons Dis. 2013;2(3):231-7. doi: [10.3233/JHD-139006](https://doi.org/10.3233/JHD-139006)
9. Goetz CG. William Osler: on Chorea: on Charcot. Ann Neurol. 2000;47(3):404-7.
10. Vale TC, Cardoso F. Chorea: a journey through history. Tremor Other Hyperkinet Mov (N Y). 2015;5:tre-5-296. doi: [10.7916/D8WM1C98](https://doi.org/10.7916/D8WM1C98)
11. Lees AJ. Noticing in neurology. Pract Neurol. 2019;19(5):427-30. doi: [10.1136/practneurol-2018-002176](https://doi.org/10.1136/practneurol-2018-002176)
12. Wexler A, Wild EJ, Tabrizi SJ. George Huntington: a legacy of inquiry, empathy and hope. Brain. 2016;139(Pt 8):2326-33. doi: [10.1093/brain/aww165](https://doi.org/10.1093/brain/aww165)
13. Critchley M. The history of Huntington's chorea. Psychol Med. 1984;14(4):725-7. doi: [10.1017/s003329170001967x](https://doi.org/10.1017/s003329170001967x)

© Instituto Nacional de Neurología y Neurocirugía
Manuel Velasco Suárez