From the archives


Brown starts by lamenting the lack of guidance available from the existing literature on what genuinely constitutes an example of Friedrich’s ‘hereditary ataxia’. He was not much helped by the comprehensive account and history of the disorder by Dr P. Ladame (Brain 1890; 12: 467–537). His starting point is that in describing ‘slow and progressive ataxy of the four limbs, usually attacking several children of the same family . . . with no authentic cases of onset after the twentieth year’. Ladame had not provided a working set of diagnostic criteria for what may be observed in clinical practice. Sanger Brown provides an illustration of his pedigree showing (despite the title of his paper) 24 affected individuals in four generations. Males and females are equally affected. Inheritance tends to pass through the female line. The proband—a Texan surveyor—presented at 28, although he probably had symptoms from the age of 14 years. Brown expresses admiration for the ‘high humanitarian spirit and untiring energy’ with which case XVIII provided details of his own and his relatives’ illnesses. Starting in the legs, his ataxy progressed to involve the arms, speech and then his swallowing. There was associated visual failure, nystagmus and bilateral ptosis. Loss of balance as young adults, visual failure and brisk reflexes characterized the phenotype of his three affected siblings. In time, other branches of the family were described. Clearly these relatives had the same disorder. Details of the youngest generation, living 2000 miles from Chicago, were made available through the help of Dr Norman Bridge in whose clinical acumen Sanger Brown evidently placed great faith. Because of the exaggerated tendon reflexes in all affected individuals, Sanger Brown preferred the description ‘hereditary ataxic paraplegia’. Taken together, he felt justified in concluding that ‘hereditary ataxy may be traced through several—at least four—generations, increasing in intensity as it descends, tending to occur earlier in life and advance more rapidly . . . it begins most frequently between the ages of sixteen and thirty five . . . as early as eleven and as late as forty-five . . . inco-ordination of the voluntary muscles . . . noticed first in the legs . . . extends to the arms, face, head and organs of speech . . .’. Sanger Brown did not describe the pathology of this disorder although he made some speculations, formulating the problem around presumed extensive degeneration of efferent motor rather than afferent pathways. In keeping with the times, he satisfied himself that galvanism improved the disabilities. He concluded that this family differed from existing descriptions of hereditary ataxia (for example in Sir William Gowers’ Manual of Diseases of the Nervous System) in the older age at onset, the exaggerated tendon reflexes and the optic atrophy. In a commentary on Sanger Brown’s paper, Dr Joseph Ormerod found himself unable to accept that the description justified extending the boundaries of definition for Freidreich’s ‘hereditary ataxy: exaggerated not absent reflexes; the absence of spinal deformity and club foot; ptosis and optic atrophy all served to separate the two conditions. The absence of pathological details was regrettable and a severe limitation. However, families described by Menzel (Archives für Psychiatrie 1891; 22: 161 et seq) and Nonne (Archives für Psychiatrie 1891; 22: 283 et seq) had provided pathological details of sibships that closely resembled Sanger Brown’s cases. Here, the striking feature was cerebellar and brainstem atrophy with loss of large nerve fibres in the spinal roots but intact long tracts: ‘possibly the want of a proper nervous development is the primary and hereditary factor’. Professor Bernhardt of Berlin rubbed in the probability that Sanger Brown’s suggestion of linking his pedigree to a form of Freidreich’s disease was an error, for much the same reasons as Ormerod. That said, he felt instinctively that there were similarities between cases in which ‘ataxy plays the chief part . . . another in which spastic elements predominate and a third where spinal atrophies and paralyses hold the field . . . but all these morbid types and other familial nervous affections . . . may be referred to faulty development’. Thus, the principles of the hereditary ataxias and related disorders were laid out; a stereotyped but often distinct clinical phenotype within families; distinct patterns of inheritance that later were given mechanistic genetic explanations moving from the simple concept of dominance to more complex features such as anticipation; the cooperation of affected individuals for tracing and describing the nature and extent of the affliction; and the requirement for pathological characterization of these disorders. After Sanger Brown, the next major development was Gordon Holmes’s papers of 1907, eventually culminating in the classical work of Anita Harding (1984).

Alastair Compston
Cambridge