Editorial.

FAMILIAL AND HEREDITARY NERVOUS DISEASE.

OUR knowledge of the large group of degenerative nervous affections, hereditary or familial as they often are, has scarcely progressed beyond the stage of mere description. In no class of disease, perhaps, has study of morbid anatomy been pushed to more barren limits or failed more signally to furnish a clue to treatment than in this, where, commonly enough, to become the victims the subjects have only to be born of the same parents and reach the age marked out by fate. Here, if anywhere, lies a problem for preventive medicine; if we knew what gives to the parents "le triste privilège de procréer de tels enfants" we might perhaps be able to neutralize the mischief at its source. Simple diagnosis of a case of pseudohypertrophic muscular paralysis, mere addition to the pathological records of Friedreich's disease, seems nothing less than futile as long as tracing the stock and investigating the progeny is ignored, or the question of determining how germ-plasm and antenatal development are warped remains unsolved. It has been asserted with some degree of truth that we know less of the blood lines of our human stock than we do of our cattle. In the 17th century three brothers sailed from England to America, and it appeared then to matter less than nothing that one of the parents suffered from hereditary chorea; but had they on that account been refused permission to land, America, in the words of Charles B. Davenport, "would have lost two leading educators, a surgeon or two, two or three State assembly men, and several ministers, and—900 cases of one of the most dreadful diseases that man is liable to, that produces individuals who for half a century know no waking hour free from forced movements, often of a violent character, and in whom often the mental functions one by one deteriorate". When, in conjunction with the embryologist, the biometrician, and the experimental pathologist, devotion on the part of the neurologist to the basic problems of nervous heredity takes the place of mere exhibition of familial cases, when morphological examination of a fifty-year-diseased brain and cord is abandoned in favour of biochemical investigation during the life of the individual,

when marriage selection ceases to be a Utopian dream, while the perpetuation of familial nervous disease becomes a reproach, only then will a genuine advance in the therapeutic direction have been made.

At present, speculation has to take the place of facts. A distinction has been drawn between the inheritance of structural or physiological anomalies recognizable at birth and remaining unchanged, and of 'tendencies' to the development of degenerative states in later life. The direct inheritance of structural trifles such as syndactyly or crooked little fingers, of physiological abnormalities like colour-blindness or left-handedness, can be worked out on a large scale in suitable families and shown to lend some support to Mendelian laws on the transmission of dominant and recessive characters; but in actual hereditary and familial nervous disease we do not know what 'tendency' really stands for, nor whether it is in the strict sense congenital. Clinical experience constantly gives us examples of one and the same familial nervous degeneration appearing either in infancy, or in adolescence, or in later life, so that the line between congenital and adult dysgenesis loses significance. From a practical viewpoint it signifies little whether a myopath has "never used his limbs properly" or only "since he was knocked on the head at school"; of greater import is the difficulty in the application of Mendelian principles to the data concerned.

Dr. Bateson, whose work on Mendelianism lends authority to his dicta, doubts whether many of the family affections are illustrations of heredity at all, in the biological sense, and suggests some may be due to "actual transmission of a disease-germ through the reproductive cells". Yet for Huntington's chorea and for some occasionally sex-limited inheritances such as peroneal muscular atrophy and pseudohypertrophic muscular paralysis, for Leber's atrophy and myotonia atrophica with or without cataract, we cannot conceive a hereditary factor to be wanting, whatever it be, and however it fail to conform to Mendelian rules.

For early and late degenerations alike the theory of 'abiotrophy' has been suggested by Gowers. Virtually identical is the theory of "premature physiological senescence of certain organic systems" of Raymond, a process whose date of onset varies with the individual and the disease and is independent of any external factor, whereas Gowers is willing to admit occasional excitation by some extraneous cause, of itself inadequate to produce the enduring effect. According to the *Ersatztheorie* of Edinger, on the other hand, degeneration ensues on insufficient repair of normal nerve-cell and nerve-fibre waste owing to defective nutrition, which in its turn is occasioned either by hereditary nervous weakness, or by injury, or the action of a toxin, as the case may be.

There are, however, difficulties in the way of acceptance of each and all of these hypotheses. To ascribe solely to muscular exertion, consequent waste, and subsequent failure of repair the proximal atrophy of the Erb myopathy and the distal atrophy of the distal type, alike, is to assume a difference of preceding muscular activity in the two instances which is unreasonable. If we believe, with Gowers and Raymond, in the congenital gift of a limited span of life for the affected systems, we are confronted with the difficulty that the degenerative process often fails to single out these in their entirety. Amyotrophic lateral sclerosis is cited as the motor neurone degenerative disease *par excellence*; but in it irregular involvement of certain sensory systems is very commonly remarked. Stress has been laid on the absence of any histological evidence of inflammatory reaction in the degenerative or familial group as an argument in favour of the abiotrophic view, but the neural atrophy that undoubtedly occurs in the so-called 'deficiency diseases' is proof of the action of other factors than abiotrophy in the production of nervous degeneration. Some familial affections, such as periodic family paralysis, or familial myoclonus-epilepsy, can indeed scarcely have any structural lesion for their basis, some autotoxic process or metabolic error being more plausible. It is surely permissible, too, to hold that morbid function may play a part in effecting structural change.

No one theory is of universal applicability in the difficult question of familial nervous disease. Occasionally direct inheritance of fixed characters may be postulated, but in most familial affections the variations are such as to frustrate any effort to explain them by the laws of heredity, and we are driven to the assumption that toxic, glandular, nutritional, and other factors may often determine the onset, decide the incidence, and prescribe the course of the disease, especially when it makes its appearance in an isolated and sporadic way.