

The opportunity to remember William Richard Gowers (1845-1915) and his concept of abiotrophy, now best understood and called apoptosis or programmed cell death

A oportunidade de rememorar William Richard Gowers (1845-1915) e seu conceito de abiotrofia, agora melhor compreendido e denominado apoptose ou morte celular programada

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ABSTRACT

William Richard Gowers (1845-1915) was one of the most prolific and insightful neurologists of all times. He gave major contributions to the development of the medicine through the presentation of signs, syndromes, new concepts and many publications, mainly based on his thorough examination of his patients at the National Hospital, London. In this paper, they were enrolled several Gowers' contributions, besides, it is discussed his concept of abiotrophy. Gowers at his time already recognized what is now most deeply understood and called programmed cell death or apoptosis that occurs normally during the development or aging, but also under a range of stimuli and conditions, physiological or pathological, on the dependence of a cell selective vulnerability.

Keywords: Gowers, neurology, abiotrophy, apoptosis, programmed cell death, semiology, death centennial.

RESUMO

William Richard Gowers (1845-1915) foi um dos mais prolíficos e perspicazes neurologistas de todos os tempos. Ele deu grandes contribuições para o desenvolvimento da medicina, por meio da apresentação de sinais, síndromes, novos conceitos e muitas publicações, principalmente com base em sua análise aprofundada de seus pacientes no *National Hospital*, em Londres. Neste trabalho, foram registradas várias contribuições, além disso, discute-se o seu conceito de abiotrofia. Gowers, na sua época, já reconheceu o que agora é mais profundamente compreendido e denominado de morte celular programada ou apoptose, que ocorre normalmente durante o desenvolvimento ou envelhecimento, mas também sob uma gama de estímulos e condições, fisiológicas ou patológicas, na dependência de uma vulnerabilidade seletiva de células.

Palavras-chave: Gowers, neurologia, abiotrofia, apoptose, morte celular programada, semiologia, centenário de morte.

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INTRODUCTION

William Richard Gowers (1845-1915) (Figure 1) was an illustrious English neurologist with a vast contribution to the neurology and he was "... an extraordinary observer, accurate and painstaking, with a wide horizon and a sound judgment..."¹ Gowers was appointed assistant physician at the University College Hospital (1872), keeping this appointment for 16 years.² Earlier (1870), he acquired the position of registrar or "assistant to the physician" at the National Hospital in London,³ but only 20 years later he became full physician, and in few years (1897) he was knighted by Queen Victoria in her diamond jubilee honors list.^{3,4} This hospital was founded in June 1860 – the first specialized hospital for neurology in the world. Gower's major contributions to neurology originate there and are unfolded afterwards. Gowers was a remarkable junior colleague of John Hughlings Jackson (1835-1911), a formidable and revolutionary thinker, and a supposed much easy-going person, but less comprehensible by the medical milieu than the first, more prone to be a writer, diagnostician and teacher.^{3,4}

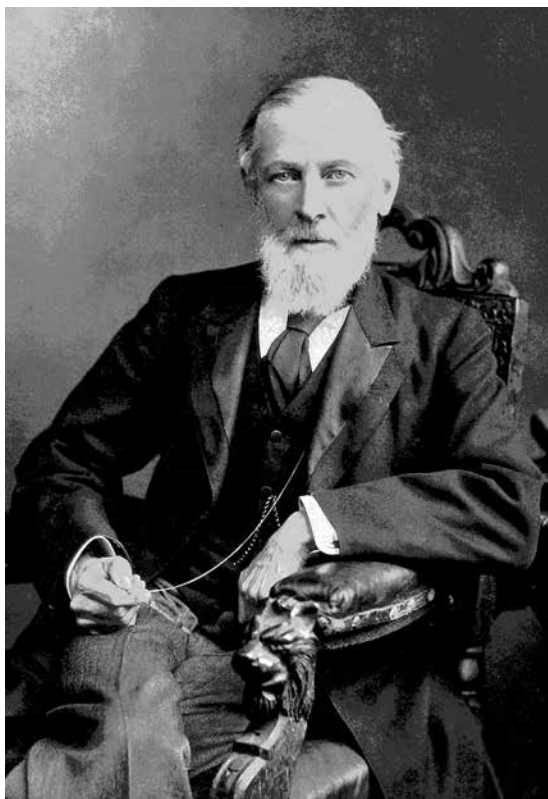


Figure 1. Sir William Richard Gowers (London, 20 March 1845-4 May 1915). Fonte: http://upload.wikimedia.org/wikipedia/commons/0/09/William_Richard_Gowers.jpg.

From 1870 to 1890, Gowers had his most productive years of research and publications when he examined and treated thoroughly patients mainly at the National Hospital.^{2,4} He recorded plenty of data in shorthand, in this way collecting an important material for his publications, as an outstanding and concise writer, and also qualified painter.^{2,4}

Gowers made several contributions to neurology, and many of them bears his name, in spite of his lack of sympathy for eponymous.³ An important assertive description and renowned sign is to confirm proximal weakness of the extensor muscles of the thighs (Gowers' sign) observed previously by Duchenne. However, Gowers gave a full description of this sign and its variants, and he realized that it would also be important in other types of myopathies, besides the one of Duchennes' muscular dystrophy.³ He correlated for the first time the relationship between the vertebral bodies and spinal levels.³ Many of the anatomical findings, signs, syndromes and chemical solutions with bears his name or are related to him are enrolled in the box 1.³⁻⁵ Gowers published several books, and the first important one was called *A manual and atlas of medical ophthalmoscopy* (1879) with the emphasis to use of the ophthalmoscope, but the worldwide famous textbook in two volumes was the *Handbook of diseases of the nervous system* (1886-8, and 2nd edition, 1892-3). Other important books were *Epilepsy and other chronic convulsive diseases* (1881) and *The borderland of epilepsy* (1907), his last book, where he described intermittent disorders similar to epilepsy, dealt with faints, vagal attacks, vertigo, migraine, and sleep symptoms, all episodic disturbances whose phenomenology could resemble but as Gowers put it, "near it, but not of it".⁶ The 1881 book on epilepsy were of outstanding importance because of its propagation of the revolutionary Jackson's concepts on epilepsy in a readable, logically argued, and largely consistent accounts of epileptogenesis what is completed in 1907.⁶ Gowers' interpretation was in part dependent on Jackson's insights, although he also incorporated some ideas from earlier workers⁶. Eadie⁶ expresses that the aspects of Gowers' papers concerning epilepsy, mainly the earlier ones, dealt with epileptic phenomenology rather than with epileptogenesis *per se*, and later were directed toward

aspects such as epilepsy and marriage, the insurability of those with epilepsy, and the inheritance of the disorder. Among Gowers' contribution, it is also included the term "the dark basement of the brain" to basal ganglia,⁴ besides the term knee-jerk, amyotatic, fibrositis.³ He also introduced the concepts of upper and lower motor neuron, and of abiotrophy (1902)^{3,7} which will be discussed in the next section in comparison with the growing understanding of what is apoptosis.

Regarding Gowers' personal life, they were given some notes about his origins and end. It is remarkable his and her mother battle against a humble cradle,⁴ but Gowers had at last the good fortune to have as mentor Sir William Jenner and John Russell Reynolds⁴ what favored the distinguished student. With regard to his failing health that destroyed him, the probable generalized arteriosclerosis obliged Gowers to retire at the age of 62. Two years previously his death, his wife, mother of his two sons and two daughters, Russell Reynolds niece-in-law, passed away.^{1,4}

Box 1. Neurological issues named after Gowers

An anatomical tract, signs, syndromes, solutions have been baptized with Gowers' name,^{3,5} besides there are signs related to him such as nasal smile of myasthenics,⁴ fixation spasms, pharyngolaryngeal nystagmus;³

Gowers' panatrophy, a disturbance manifested by development of clearly defined areas of atrophy of skin with loss of subcutaneous tissue, more prevalent in women;^{4,5}

Gowers' phenomenon or Gowers' ischias symptom, clinical sign in ischias by passive dorsiflexion of the foot that causes pain along the sciatic nerve when the former is constricted;⁵

Gowers' ptosis, a bent forward of the head when sitting upright;⁵

Gowers' sign or Gower's manoeuvre, a clinical sign of muscle proximal weakness mainly found in muscular dystrophy in childhood;^{3,5}

Gowers' syndrome II or Paton's syndrome or Gower's symptom, irregular contraction of pupil as a precocious sign of tabes dorsalis;⁵

Gowers' syndrome III, attacks of paraesthesia, dyspnoea, precordial discomfort in the form of pain or palpitation, depressed pulse, pallor, cramps, and a feeling of apprehension and dread, that Gowers applied the adjective "vagal", now considered psychogenic;⁵

Gowers-Welander syndrome, Gowers' syndrome or Welander's syndrome, a distal muscular dystrophy observed in Sweden, occasionally in other areas;⁵

Gowers-Paton-Kennedy syndrome or Kennedy's syndrome or Kennedy's phenomenon, unilateral ipsilateral atrophy with contralateral papilloedema, central scotoma, and anosmia;⁵

Gowers' tract or Gowers' bundle, the anterior spinocerebellar area revealed in collaboration with a pupil the neurosurgeon Victor Horsley;^{3,5}

Gowers' mixture for treating migraine headaches, composed of liquor trinitrini, sodium bromide, tincture of gelsemium, tincture of nux vomica (containing strychnine), dilute nitri cor hypobromic acid, and chloroform water;⁴

Gower' solution, dilution of sodium sulphate and acetic acid for counting hematias.⁵

Abiotrophy vs apoptosis

Gowers gave major contributions for the neurology, and he explained in the best way at the moment, for practical purpose, his theory of abiotrophy (1902),⁷ precursor of the one of the programmed cell death or apoptosis,⁸ a concept of acute, but also chronic cell death existing, *e.g.*, in some chronic neurodegenerative diseases.⁹ This link was also given by Daniel *et al.*⁹ "Abiotrophy, pathoklisis and other synonymous have recently undergone intellectual resurrection emerging as the concept of apoptosis now synonymous with programmed cell death". A remark to be done is that pathoklisis was coined by Cecile and Oskar Vogt (1925), *apud* Daniel.⁹ Naturally, this relationship may be now more well evaluated by means of animal models and molecular biology.

Gowers in his lecture (1902) about *Abiotrophy: diseases from defect of life*⁷ (excerpt, Box 2) stated that many degenerative diseases of the nervous system are a result of a defect in vitality. "...We do not, indeed, apply the Word 'death' to this slow decay of the elements; we speak of it as 'degeneration', but the process is in many cases, perhaps in most, an essential failure of vitality and I think it is instructive to consider the degenerations in this aspect." For him the understanding of what he called abiotrophy was important for practical reason because "it may sometimes save from waste of money that can ill be spared, and from the waste of hope which means only deeper disappointment". Naturally, 113 years ago this was all that he could say about apoptosis, before the development of molecular genetics. The abiotrophic definition by Gowers has its correspondence now to apoptosis, often used synonymously with programmed cell death, which involves the genetically determined elimination of cells.⁹ Various morphological changes occur marked by shrinkage of the cell and piknosis that is the result of chromatin condensation – the most characteristic feature of apoptosis, but there are also necrotic-like phenotypes that require gene activation and protein synthesis as presented by Elmore.¹⁰ The search on PubMed, system gives a glimpse of the development of this concept from the scarce 143 papers that included the term abiotrophy (title/abstract), from 1939 forward, to one of 244553, apoptosis. This last was first registered in 1972 about the "*Apoptosis: a basic biological phenomenon with wide-ranging*

implications in tissue kinetics” by Kerr, Wyllie and Currie, *apud* Elmore.¹⁰ However, in the veterinarian literature the term abiotrophy and apoptosis is largely used^{11,12} (Box 2). Anyway, the chronic evolution of some human diseases also involves apoptosis, and several studies presently indicate that apoptosis might occur and contribute, *e.g.*, to Alzheimer disease onset and progression.¹³

Box 2. Gowers’ reasoning about what he called abiotrophy, now known as programmed cell death or apoptosis, in *Abiotrophy: diseases from defect of life*⁷

Gowers’ understanding about abiotrophy: “...besides this general life, the termination of which involves that of every part of the body, many of these parts have their own vitality. Some of them may slowly die, while the life of all the rest goes on without impairment. They may die from many causes, some early, inevitably, from a grave defect of vital endurance; some much later, the failure being only slightly premature; and some at various times, apparently from various causes. When the failure is early it is often due purely to a defect in vitality, a defect which seems to be inherent, the tendency there to inborn”. “We do not, indeed, apply the word ‘death’ to this slow decay of the elements; we speak of it as ‘degeneration’, but the process is in many cases, perhaps in most, an essential failure of vitality, and I think it is instructive to consider the degenerations in this aspect.” “...Here the simplest mode of obtaining what we need is to insert the root of βίος after the negative particle in ‘atrophy’ which gives us ‘abiotrophy’.” After these reasonings, Gowers classified the types of abiotrophy, mainly according to the localization (cutaneous, muscular or in the nervous system) or period of life (precocious or later), besides some definite cause. Regarding Later Neural Abiotrophy, he gave this example: “Another senile malady, paralysis agitans, must be referred to vital failure in some cerebral motor structures. In its conditions and course, it is a striking example of a cerebral abiotrophy”. He also distinguished inherent vitality from functional vitality, *e.g.*, a close vital relation between the muscular and nervous structures. He considered that many forms of abiotrophy in the nervous system, perhaps the most striking is one of which these spinal motor neurons are the seat. “A third group of degenerations remains, large and important. They are the varied degenerations that occur, especially in middle life, as the result of some definite cause.” “It is not clear how far these are due to a defect of life. The degeneration may be the result of the presence in the blood of some material which is able to enter into the constitution of the nerve elements, but is not adequate for their proper functional or structural maintenance. They may slowly recover if the supply of the noxious matter ceases. Arsenical neuritis is an example.” Gowers recognized that “Their nature is easily discerned when they occur in groups which have the tie of consanguinity, but the discernment is less easy when the diseases occur in isolated form.”

Elmore¹⁰ reviewed the concept of apoptosis and reinforced much of what was presented by Gowers, as seen above, because apoptosis, a cell programmed death occurs: normally during development and aging; also, as a defense mechanism such as in immune reactions or when cells are injured by disease or noxious agents, but a range of stimuli and conditions, both physiological and pathological, can generate it, in a cell selective vulnerability. The veterinarian literature presents plenty of proofs of this association, abiotrophy vs apoptosis, as seen in the paper by Blanco *et al.*¹¹: “...the occurrence of apoptosis in this cell population was investigated by... Both optical and electron microscopical images showed a scant number of Purkinje cells, most of them with morphological features of apoptosis...” This is mainly found in horses, as Arabians and purebred Arabian horses, but also in other species. Nonetheless, cerebellar abiotrophy does not have the same aetiology as in the horse, where a single autosomal recessive locus is assumed to be responsible for the disease, as referred by Cavalleri *et al.*¹²

CONCLUSION

Gowers was an industrious and insightful neurologist, besides a skilled writer, and a talented painter. He explained in the best way at the moment, for practical purpose, his theory of abiotrophy, precursor of the one of the programmed death cells. Here, it is offered our homage to this outstanding neurologist in his death centennial.

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CONFLICT OF INTEREST

None.

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