

## COMMENTARY

# Brown-Séguard, Father of Endocrinology

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Famous for the eponymous syndrome of hemisection of the spinal cord, Brown-Séguard was born in Mauritius and, in this 125th anniversary year of his death in Paris in 1894, it is apt to review his achievements as the undisputed father of endocrinology. He abandoned a lucrative private practice in London for an international academic career emphasising an experimental approach. Pioneering the discipline of endocrinology through self-experimentation, he freely distributed his preparations for male hormonal replacement therapy to promote their evaluation. Whereas their perceived effectiveness was due to a placebo effect, his contribution was central in the development of endocrinology.

Brown-Séguard had an enquiring mind and never missed an opportunity to exploit circumstances for pursuing issues whether for observational or interventional purposes. His eccentric personality was associated with bouts of depression, likely with bipolar disorder<sup>1</sup>, and frequent moves: he settled six times in France and four times in America besides undertaking two journeys to Mauritius where the setting was not propitious for carrying out tasks of professional interest<sup>2</sup>. This roving character led to more than 60 transatlantic crossings and about six years at sea. He had royalty as patients, Charles Darwin and Louis Pasteur as close correspondents, and influenced his neighbour Robert Louis Stevenson for the plot of *Dr Jekyll and Mr Hyde*.

### *Transatlantic career*

Born in Port Louis in 1817, Edouard Brown-Séguard never knew his father, an American sea

captain who died during the pregnancy. He was raised by his French mother, partly of an Indian descent, in a deprived environment in Port Louis. Sponsored for a literary career by local benefactors who had recognised his academic potential, he was unsuccessful as an author in Paris where he subsequently enrolled for medical studies.

His peripatetic career included prestigious appointments as a founding physician at the National Hospital in Queen Square in London and professor at the Collège de France and Harvard University<sup>3</sup>. He even turned down a professorship in Geneva. Having openly expressed aversion to slavery during a professorship in Virginia<sup>4</sup>, he faced racial discrimination due to his physical traits suggestive of Indian ancestry.

### *Experimental research*

Having observed injuries sustained by sugarcane cutters during his five-month stay in Mauritius in 1843, he investigated nerve damage for his graduation dissertation of 1846, at the age of 28, and described the syndrome of hemisection of the spinal cord only three years later in 1849. His observational inquiries were complemented by interventional experiments especially on animals ranging from dogs and cats, through guinea-pigs and salamanders, to the tenrec Mauritian hedgehog. As an avid researcher, he worked extensively from home to the extent that his house, in Cavendish Square in central London, resembled a menagerie. With an acrimonious debate from the virulent ire of the antivivisection movement, he preferred to bear the brunt from that lobby rather than explaining the importance of seemingly

unrelated experiments thereby divulging his research strategy.

Committed to self-experimentation, he swallowed vomit from patients during the 1854 epidemic of cholera in Mauritius to test hypotheses on the aetiology, transmission and treatment of the disease and, much later aged around 70, injected himself subcutaneously with animal gonadal concoctions in the quest for hormonal replacement therapy.

### ***Hormonal theory***

Following the description by Addison of the clinical picture of adrenal deficiency, Brown-Séquard promptly experimented on various animals. A year later, in 1856, he demonstrated that removal of the adrenals was fatal, and pursued research on his idea regarding their essential role. The pioneering step for recognition of endocrinology as a scientific discipline occurred in his series of medical lectures in Paris in 1869 when he postulated the crucial role of the release, into the bloodstream, of “internal secretion” by several glands. In 1875, he specifically alluded to a possible role for animal extracts as replacement therapy for dysfunctional adrenals and “sexual glands”.

His presentation of 1 June 1889, at the meeting of the Société de Biologie in Paris, on the value of animal testicular extracts to control the ageing process is recognised as the foundation of the endocrinology as reaffirmed in 1989 at the centennial anniversary celebration of the specialty<sup>5, 6</sup>. This communication influenced others to demonstrate, within two years, the value of thyroid extract for treating myxoedema and an elegant follow-up that led to the identification of thyroxin.

The quest for rejuvenation therapy involved the interface between science and morality by going beyond brain control of the nervous system to address personal decisions on sexual intercourse through an elixir for recovering sexual prowess. His nascent efforts in reproductive endocrinology were strongly opposed by societal attitudes towards sex and sexuality thereby impeding the emergence of both reproductive sciences and promising applications for hormonal replacement therapy. Having been upset, moralists

ridiculed his concoctions for a fountain of youth by making allusions to pentacle, magic and quackery.

### ***Hormonal replacement therapy***

Brown-Séquard investigated the potential of concoctions of water-based crushed extracts from animal gonads and blood from gonadal veins, to regain vitality. His experiments with ovarian extracts did not lead to effective products. In 1889, he reported personal benefits from subcutaneous injections of aqueous testicular extracts from dogs and guinea pigs: improved wellbeing including “facility of intellectual labour”, stronger muscles and a 30% increase in his jet of urine<sup>7</sup>.

Regretting that his earlier self-experimentation had been “at first so completely misunderstood”, Brown-Séquard distributed his elixir of life for free to medical practitioners in various countries, conditional upon receiving feedback on the outcome of treatment<sup>8</sup>. The perceived value of his formulation led international pharmaceutical companies, entrepreneurs and charlatans alike to market potions for eternal youth. Besides it gave an impetus to the organotherapy movement which promoted the treatment of various diseases with extracts of organs and tissues from various animals<sup>9</sup>. However this frenzy of activity was short-lived as research findings from endocrinology soon discredited claims of organotherapy which was then abandoned as a discipline<sup>10</sup>.

The important lesson to be learned from the popularity of this elixir of youth pertains to the need for increased awareness of the placebo effect of medical treatment. The aqueous testicular extracts, as prepared by Brown-Séquard, could not have been effective simply because of the poor solubility of sex hormones in water, success of his preparations being attributed to a marked placebo response<sup>11</sup>. The situation is relevant today to avoid the empirical use of testosterone in the absence of specific indications<sup>12</sup>. Whereas the ideas of Brown-Séquard were far ahead of his times, he was at a major disadvantage from the absence of appropriate methods for his investigations. Nevertheless he was instrumental for progress by

opening avenues for novel approaches in endocrinology.

### ***Moving forward***

Much of our understanding of female reproductive physiology resulted from massive research funding, from the 1950s, in the quest for female methods of contraception to control overpopulation. Despite advances in reproductive endocrinology and prominence of gender concerns, there has been uneven progress in international sexual and reproductive health over the last 25 years<sup>13</sup>: the major disadvantage of male, as opposed to female, sexual and reproductive health care is exemplified by the lack of service applications for cancer screening, hormonal contraception and replacement therapy for men.

The above gaps will only be overcome through the allocation of resources for research and development, including biomedical aspects, which are much neglected in international health with its focus on service delivery. Rigorous studies on male reproductive health are necessary to ensure that only effective interventions are implemented at the population level.

### **Conflict of Interest**

None.

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