

What's in a Name? Henry Dale and Adrenaline, 1906

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By the beginning of the twentieth century the use of widespread advertising, trade names, and specialized marketing techniques was a distinctive feature of the commercial world. These attributes were well developed in the trade in medicines, a field that ranged from quack cures and secret remedies through proprietary brands to "ethical pharmacy".¹ The British pharmaceutical firm, Burroughs, Wellcome & Co. had, by that time, achieved considerable success in promoting itself as an ethical company guided by scientific principles and remote from the quackery and chicanery of pill peddlers and nostrum-mongers. A component of that ethical behaviour was the maintenance of their own production and advertising standards and the proper recognition of others' commercial rights.

In the final decade of the nineteenth century Burroughs, Wellcome & Co. had established quasi-independent laboratories, the Wellcome Physiological Research Laboratories (WPRL), in which physiologists and pharmacologists were employed to undertake basic research not directly or necessarily associated with the company's commercial enterprises. One such scientist was the future Nobel Laureate Henry Dale, who in 1906 wished to publish a paper in which the word "adrenaline" appeared.² This was then the commonly accepted term, within Britain's physiological community, for the active principle of the suprarenal gland. However, the word "Adrenalin" was a registered trademark of the American pharmaceutical firm Parke, Davis & Co., and Dale's intended use was forbidden by Henry Wellcome. Dale and his colleagues refused to accept this injunction, and the ensuing debates raised important issues within the Wellcome

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¹ The campaign against "secret remedies" was spearheaded by the *British Medical Journal*, see P W J Bartrip, *Mirror of medicine: a history of the British Medical Journal*, Oxford, Clarendon Press, 1990, especially pp. 189–202.

² For Dale see W S Feldberg, 'Henry Hallett Dale 1875–1968', *Biog. Mem. of FRS Lond.*, 1970, 16:77–174, and also E M Tansey, 'The early scientific career of Henry Dale, FRS, (1875–1968)', PhD thesis, University of London, 1990, *passim*.

organization, and beyond.³ These included technical questions of chemical and physiological nomenclature, and legal concerns about trademarks and trade names. They also brought into sharp focus the then novel relationship between research laboratories and commercial companies, and raised serious questions about scientific authority within several laboratories that were part of the Burroughs, Wellcome empire. The episode also illustrates difficulties that faced scientific workers associated with commercial enterprises, in addition to providing an insight into the personal and scientific motivation and development of Dale's distinguished career.

This paper focuses on just six weeks during 1906, following the transmission to the Company headquarters of Dale's request to use the word adrenaline, during which office and scientific staff employed by Wellcome, and outside advisers and official bodies, all became embroiled in the affair.

The correspondence on this matter is scattered throughout the Archives of the Wellcome Foundation and the Wellcome Institute, and also in the private papers of some of the participants. The principal correspondents were Henry Wellcome, who was abroad for most of the period; Henry Dale of the WPRL, and his director Walter Dowson; and staff from their sister organization, the Wellcome Chemical Research Laboratories (WCRL), most notably Dr Hooper Jowett. Much of the correspondence was channelled through George Pearson, the Managing Director of the Company, and clerical staff at the Company's offices usually prepared additional copies, which were then circulated to all other interested parties. This complicates matters, since much of the communication took place obliquely, as illustrated in a letter written by Henry Dale which begins: "Dear Mr. Wellcome, Dr. Dowson has handed me a copy of your recent letter to Mr. Pearson . . .".⁴ More than forty letters and memoranda were written during this period, and several copies of the same letters have been found in different locations, each annotated by their respective recipient. It is from all these papers and their annotations that the following account has been constructed.

The Wellcome Physiological and Chemical Research Laboratories

The original laboratory, which became the Wellcome Physiological Research Laboratories, was established in 1894 to produce the new "biological" therapeutics, the serum anti-toxins.⁵ This initiative was very much the brainchild of Henry Wellcome, who

³ The word "Adrenalin" with and without the initial capital and the final "e" was used almost interchangeably in the publications and private correspondence cited in this paper. There does not appear to have been a sharp distinction between the usages, and although the former was used more often to refer to the Parke, Davis product, its use was not consistent.

⁴ Dale to Wellcome, 22 Feb. 1906. Henry Wellcome Archives in the Wellcome Institute for the History of Medicine Library, henceforward WIHM:HSW.

⁵ Some of the other influences on the development of the British pharmaceutical industry, in particular its relationship with the dye industry, are explored in L F Haber, *The chemical industry during the nineteenth century: a study of the economic aspect of applied chemistry in Europe and America*, Oxford, Clarendon Press, 1958, especially 'Chemical manufacturers and their problems', pp. 186–230; and R Stolz and R Schwaiberger, 'The correlation between dye chemistry and pharmacy in creating the modern chemotherapy', *Hist. Tech.*, 1987, 3:193–203. E M Tansey, 'The Wellcome

played a close personal part in their creation, promotion and subsequent activities. Wellcome, a trained pharmacist from America, had, with Silas Mainville Burroughs, founded a pharmaceutical company in Britain, which rapidly established a reputation for scientific thoroughness and accuracy, largely owing to its range of pharmaceutical preparations marketed under the trade name of “Tabloid”, an elision of tablet and alkaloid. These precisely tableted, formulated and standardized compounds were enormously successful. They were vigorously, even aggressively, marketed by the Company, and the trade name was rigorously protected, often by recourse to the law.⁶ The Tabloid range was a substantial part of the “scientific” image that the Company eagerly and successfully projected. Its advertising material stressed the scientific orientation of the firm and, from the very beginning of the company’s existence, publicized the existence of laboratories and specialized departments within the factories. These were almost certainly associated with manufacturing processes in some way, rather than with innovative research activities, although it is worth remembering the caution,

that what one man may describe as a ‘research laboratory’ another may, with apparently equal authority, call a development department. Who is to say, when we are dealing with organisations of eighty or more years ago, which description is correct?⁷

The comment is particularly relevant to the Wellcome organization, as several, variously designated laboratories were created throughout the 1890s and the early decades of the twentieth century. Many of them were situated within the firm’s factories, but two, the WPRL and WCRL, were explicitly encouraged to undertake research work, and, the Company maintained, they were independent of commercial activities and run on strictly scientific lines.⁸ Despite that assertion, the *raison d’être* of the Wellcome Physiological Research Laboratories had been the production, standardization and packaging of anti-toxin therapies, which were subsequently marketed by the parent pharmaceutical company. The links between the WPRL and Burroughs, Wellcome & Co. were therefore close, although those between the Company and the WCRL were even more intimate.

The Wellcome Chemical Research Laboratories were founded a year after the Physiological Laboratories, in February 1895, when, in the midst of proceedings to dissolve their partnership, Silas Burroughs died and Henry Wellcome became sole owner of the company. Eight days after his partner’s death, Wellcome wrote to a former American college contemporary of his, Dr Frederick Power,⁹ inviting him to London, promising,

Physiological Research Laboratories 1894–1904: the Home Office, pharmaceutical firms and animal experiments’, *Med. Hist.*, 1989, 33:1–41, emphasizes the specific situation of the Wellcome organization.

⁶ Wellcome had several legal battles to reinforce his trademarks, especially “Tabloid”, see G Macdonald, *In pursuit of excellence*, London, Wellcome Foundation, 1980, p. 12; H Turner, *Henry Wellcome: the man, his collection and his legacy*, London, The Wellcome Trust and Heinemann, 1980, pp. 14–15; R Rhodes James, *Henry Wellcome*, London, Hodder & Stoughton, 1994, pp. 112–13, 292–3.

⁷ D S L Cardwell, *The organisation of science in England*, London, Heinemann, 1972, pp. 175–6.

⁸ The independence of the labs seems highly questionable: they were funded as integral components of the Burroughs, Wellcome Company; their staff were recorded as company employees; and they were administered by staff from the Company headquarters. For further details see Tansey, *op. cit.*, note 5 above, pp. 35–6.

⁹ For biographical details see J Parascandola, ‘Frederick Belding Power’, *Dictionary of scientific biography*, 14 vols, New York, Charles Scribner’s Sons, 1970–80, vol. II, pp. 120–1.

to fit up for you a most thorough and complete experimental laboratory near my offices, . . . I want you for constant consultation as I propose to enter much more into scientific medical chemical products. . . . I should not ask you to take up any business cares or actual manufacturing drudgery but only experimental and strictly scientific work etc such as I know is most congenial to you.¹⁰

Power accepted this attractive offer, and in July 1895 the opening of the “Wellcome Research Laboratories” was celebrated in London with a resounding declaration from Wellcome that they were quite distinct from his business. Although he hoped that they might contribute something of value to him and to the wider world, “[T]he work”, he announced, “is to be carried out on no selfish lines . . . controlled and dictated with the highest regard for science.”¹¹

The Chemical Laboratories had a particularly close relationship with Wellcome and the Company: the Director, Power, was a distinguished chemist and an old and valued friend of Wellcome; the WCRL were physically situated next door to the Company headquarters in the City of London; and their research was traditional analytical chemistry, the experimental isolation, identification and, ultimately, the synthesis of new chemotherapeutic compounds, the kind of work that Wellcome himself understood well. In contrast, the scientific staff appointed to the WPRL were not distinguished figures in medical research; the laboratories, originally in central London, were relocated in 1899 to South London, some distance from the Company headquarters in the City; and the nature of their work was essentially innovative, and moved ever further away from Wellcome’s own direct experience.¹² In 1901 Wellcome endeavoured to expand the experimental possibilities at the WPRL by applying for them to be registered with the Home Office, under the terms of the 1876 Cruelty to Animals Act, as a place where animal experiments could be performed. After a lengthy, and at times acrimonious, debate with the Home Office, Wellcome finally obtained permission in 1901 for the WPRL to be registered.¹³ This opened up exciting new possibilities for original research in experimental physiology and pharmacology,¹⁴ and in 1904 Wellcome sought advice from Ernest Starling, Professor of Physiology at University College London, about a suitable person to work in his labs:

You will, I am sure, understand my anxiety—in view of the prospective importance of the work of this Institution—to secure the services of a man who is capable of broad and deep thinking, who has fertility of mind, originality and alertness, and patient persistence; a man who will concentrate his whole mind and energies on this work. I want the work in these laboratories to be done on the highest scientific lines and with such thoroughness and precision that it will stand the test of time and the keenest criticism.¹⁵

¹⁰ Wellcome to Power, 14 Feb. 1895, The Wellcome Foundation Ltd Group Archives (henceforward TWFL), Acc 82/1:box 12.

¹¹ ‘Dinner to Dr Power: new research laboratory in London’, *Pharmaceut. J.*, 1896, 3:78–9.

¹² E M Tansey and R C E Milligan, ‘The early history of the Wellcome Research Laboratories, 1894–1914’, in J Liebenau, G J Higby and E Stroud (eds), *Pill peddlers: essays on the history of the pharmaceutical industry*, Madison, WI, The American Institute for the History of Pharmacy, 1990, pp. 91–106.

¹³ Tansey, op. cit., note 5 above, *passim*.

¹⁴ Until that time the WPRL had been principally engaged in routine anti-toxin production and bacteriological diagnosis, as detailed in Tansey, op. cit., note 5 above, pp. 3–5.

¹⁵ Wellcome to Starling, 2 June 1904, TWFL:LB7 Letter Book personal, 1903–1904, p. 399. Starling was a little uneasy about the relationship of the WPRL to the commercial company, although he did recommend Henry Dale.

Henry Dale and Adrenaline, 1906

On Starling's advice, Wellcome offered a young Cambridge trained physiologist, Henry Dale, the position of staff pharmacologist at the WPRL. Despite the poor possibilities of obtaining a permanent position in the academic world at that time, Dale was warned about association with a commercial manufacturer by Cambridge friends, who counselled him against "selling my scientific birthright for a mess of commercial pottage".¹⁶ Dale, however, needed a job as he wished to marry, he wanted to stand on his own feet scientifically, and the WPRL offered superb facilities for research, unhampered by teaching. He accepted Wellcome's offer, and never regretted the decision.¹⁷

Thus, by the beginning of the twentieth century, Henry Wellcome had established two ostensibly private laboratories, one in physiology, one in chemistry, with designated Directors and employing growing numbers of scientifically trained staff. Both labs were lavishly equipped with gas, electricity, water, telephones and the most modern fittings and sophisticated equipment then available, and there were few routine, and no teaching, obligations for their staffs. But, as suggested by Dale's diffidence when offered employment, there were problems attracting suitable people to work in laboratories connected, however remotely, with commercial interests. It should be emphasized here that Henry Wellcome's initiatives in this direction were unique in Britain: no other pharmaceutical manufacturer had developed scientific research programmes, and explicit associations between trade and academe were virtually non-existent.¹⁸ The problem of recruitment was especially acute in the WPRL as those with appropriate scientific expertise in physiology, pharmacology and bacteriology were medically qualified, and connection, however indirect, with a commercial company was not encouraged by the medical authorities.¹⁹ Additionally, within the Wellcome organization, the scientific staff from the research laboratories were regarded as ordinary company employees. Their contracts stipulated precise working hours; a paltry annual leave with no allowance for attendance at scientific meetings during working hours; and a requirement, when necessary, to test and validate company products. Ripples of dissatisfaction regularly surface in the company records as the management tried to deal with new staff and new situations which did not easily conform to their working regulations. The contractual obligations regarding communication and publication are of particular relevance to the debate about the word adrenaline:

It is understood that you are to treat as strictly confidential, and respect as my property, all my manufacturing processes, formulae, apparatus etc. and all improvements therein, and also any inventions or new discoveries which may be made by you or anyone else in my employment; on the understanding that I shall not extract from you with respect to any discovery a confidence which is contrary to the ethics of your profession. It is also understood that before publishing any communications upon physiological matters or upon any work connected with the laboratories you

¹⁶ H H Dale, 'Autobiographical sketch', *Perspec. Biol. Med.*, 1958, 1:125–37, quote on p. 129; E M Tansey, 'Funding medical research before the creation of the Medical Research Council', *J. R. Soc. Med.*, 1994, 87:546–8.

¹⁷ Dale, *ibid.*

¹⁸ See E M Tansey, 'The founding of the Wellcome Physiological Research Laboratories: conflict or concord in medical research', in K Arnold and E M

Tansey (compilers), *Pills and profits: the selling of medicine since 1870*, an exhibition catalogue, London, The Wellcome Trust, 1994, pp. 4–16.

¹⁹ Some of the prejudices of the Royal Colleges of Physicians, and of Surgeons were expressly articulated during Wellcome's campaign to get the WPRL registered for animal experimentation, see Tansey, *op. cit.*, note 5 above, pp. 23–6.

are first to submit same to and obtain the approval of the Director. The two clauses just written refer to work done at any time either in or out of the Laboratories.²⁰

These internal regulations were reinforced by external restrictions in publishing work from the Wellcome laboratories. Some “controversy with respect to the publication of papers” arose with the *Pharmaceutical Journal*, as the Pharmaceutical Society regarded scientific papers from Wellcome staff as advertisements for the company; and whilst the *British Medical Journal* agreed to publish Wellcome papers, they refused to provide reprints that could be used for publicity.²¹

Adrenalin or Epinephrine?

Thus, in accordance with his contract, when Dale prepared a paper for publication in 1906 he passed the manuscript to his Director, Walter Dowson, for approval.²² The paper, on the physiological and pharmacological effects of ergot of rye included experiments using adrenaline, and it came to Wellcome’s attention. He objected to the use of the word adrenaline because Adrenalin was a registered trade-name of Parke, Davis & Co.²³ Wellcome suggested instead that the word epinephrine should be used, as that was how the WCRL denoted what he believed was the same chemical substance. Dale maintained that within the British physiological community adrenaline was used to describe the physiologically active principle of the adrenal glands, and did not imply a specific commercial preparation. He considered epinephrine to be inappropriate and inaccurate, and refused to use it instead of adrenaline.

So, in addition to the commercial and legal problems, there were apparently significant, technical disagreements between the chemists and physiologists about the nature of the extract of the suprarenal gland. Why was this a contentious issue? The physiological effects of a gland extract were first reported in 1894, when a north-country medical practitioner, George Oliver, visited the Professor of Physiology at University College London, Edward Schäfer.²⁴ Oliver’s personal experiments with an extract of the suprarenal glands of various animals had revealed an effect on blood pressure and arterial diameter. The two men collaborated on a series of animal experiments in which they

²⁰ Wellcome to John Mellanby, 1 Jan. 1902, TWFL:LB17, Letter Book 1901–Feb. 1902, p.441.

²¹ Wellcome to Dowson, 31 Oct. 1904, TWFL:LB8, Correspondence Personal 6 (1904–5), p. 188; 11 May 1905, *ibid.*, p.488; British Pharmaceutical Conference, Minutes of Executive Committee, 1887–1911: 24 June 1904, pp. 268–9, 8 Aug. 1904, p. 270; 8 July 1907, p. 318. For the *British Medical Journal* see, Wellcome to members of the BMA Council, 21 Nov. 1900, TWFL:LB14 Letter Books 1900–1901, pp. 468, 468a; Fauke to Jowett, 1 Nov. 1900, *ibid.*, p. 470; Fauke to Power, 3 Nov. 1900, *ibid.*, p. 471.

²² Dowson to Wellcome, 2 Feb. 1906; Wellcome’s comments, 5 Feb. 1906; both in TWFL: Acc 82/1.Box 23 ‘WPRL 1895–1922’.

²³ The use of distinguishing trade names and branded goods had developed especially during the

latter part of the nineteenth century, as commercial markets and press and poster advertising expanded, see, e.g., T Richards, *The commodity culture of Victorian England: advertising and spectacle 1851–1914*, Stanford University Press, 1990, *passim*.

²⁴ Accounts of the early experiments done on extracts of suprarenal glands by Henry Dale are based on the tradition that Oliver first recorded a vasopressor effect by injecting extract into his young son, see H H Dale, ‘Natural chemical stimulators’, *Edin. med. J.*, 1938, 45:461–80; *idem*, ‘Accident and opportunism in medical research’, *Br. med. J.*, 1948, ii:451–5. The legitimacy of the account is questioned by H Barcroft and J F Talbot, ‘Oliver and Schäfer’s discovery of the cardiovascular action of the suprarenal extract’, *Postgrad. med. J.*, 1968, 44:6–8, who provide an useful exposition of the early experimental work.

demonstrated the effects of the extract when injected into anaesthetized animals. Particularly marked was the constrictor (pressor) effect on the arterial system, which resulted in raised blood pressure. Within a year they gave two presentations to the Physiological Society, and publication of the discovery and its therapeutic possibilities in haemostasis and in adrenal deficiency (Addison's disease) stimulated the search for a pure extract of the active principle.²⁵

An initial priority was to identify the chemical composition of the active principle, and as early as 1895 two of Schäfer's colleagues began chemical analyses of the material, continuing, like all workers in the field, to use the cumbersome phrase "physiologically active extract of the suprarenal glands".²⁶ Others too were searching for the principle: the German chemist Fraenkel suggested that it was a substituted catechol, probably a benzoyl derivative, which he called spymogenin, and Abel and Crawford of Johns Hopkins University succeeded in isolating benzoate and sulphate derivatives from the gland.²⁷ In 1899 Abel²⁸ published a major paper announcing an extract which he named "epinephrin" and von Fürth isolated a similar compound, which he called "suprarenin".²⁹ Physiologically, however, neither of these two chemicals had the same activity as the crude extracts of the suprarenal gland.³⁰ In 1900 the industrial chemist Jokichi Takamine realized, after visiting Abel's lab, how to overcome the existing contamination problems, and rapidly developed a further purification stage. He patented the techniques, and arranged for Parke, Davis & Co. to market the pure crystalline substance as "Adrenalin",

²⁵ G Oliver and E A Schäfer, 'On the physiological action of extract of the suprarenal capsules', *J. Physiol.*, 1894, 16: i-iv; *idem*, 'On the physiological action of extract of the suprarenal capsules', *ibid.*, 1895, 17: ix-xiv; a full paper published later in the year contained work from both earlier communications plus new results, *idem*, 'The physiological effects of extracts of the suprarenal capsules', *ibid.*, 1895, 18:230-76. Oliver was one of the first to suggest that an adrenal gland extract could be used to treat Addison's disease, see G Oliver, 'On the therapeutic employment of the suprarenal glands', *Br. med. J.*, 1895, ii:653-5. A copy in the Wellcome Institute Library, originally belonging to Burroughs, Wellcome & Co. is marked in the margin, probably by Henry Wellcome.

²⁶ B Moore, 'On the chemical nature of a physiologically active substance occurring in the suprarenal gland', *J. Physiol.*, 1895, 17: xiv-xvii, thought that the active principle was a pyridine derivative; D N Nabarro, 'The proteids of suprarenal capsules', *ibid.*, pp. xvii-xviii.

²⁷ S Fraenkel, 'Physiological action of supra-renal capsules', *J. Chem. Soc. Abstracts*, 1897, 72:63-4, from *Wien. med. Blätter*, 1896, 14; J J Abel and A C Crawford, 'On the blood-pressure-raising constituent of the suprarenal capsule', *Johns Hopkins Hosp. Bull.*, 1897, 8:151-7.

²⁸ H H Dale, 'John Jacob Abel 1857-1938', *Obituary notices of Fellows of the Royal Society*, London, Royal Society, 1939, vol. 2, pp. 577-85; Abel's contributions to American pharmacology are

covered by H H Swain, E M K Geiling and A Heingartner, 'John Jacob Abel at Michigan: the introduction of pharmacology into the medical curriculum', *Univ. Michigan med. Bull.*, 1963, 29:1-14; J Parascandola, 'John J Abel and the early development of pharmacology at the Johns Hopkins University', *Bull. Hist. Med.*, 1982, 56:512-27; *idem*, *J.J. Abel and the development of American pharmacology: the shaping of a discipline*, Baltimore, Johns Hopkins University Press, 1992, especially pp. 57-8; and J W Fisher, 'Origins of American pharmacology', *Trends in pharm. Sci.*, 1986, Feb., pp. 41-5.

²⁹ See the references given in footnotes 63, 64 and 65 below, and O von Fürth, 'The catechol-like substance of the suprarenal', *J. Chem. Soc. Abstracts*, 1900, 78:292, from *Z. Physiol. Chem.*, 1900, 29:105-23. Some of these efforts are developed in H W Davenport, 'Epinephrin(e)', *Physiologist*, 1982, 25:76-82, an article which details some of the commercial difficulties in America that were encountered with Adrenalin(e). W Sneader, *Drug discovery: the evolution of modern medicines*, Chichester, John Wiley & Sons, 1985, ch. 6, 'Drugs affecting nervous transmission', especially pp. 96-9, also examines the chemical work on adrenaline.

³⁰ Abel's original, physiologically less active, extract was a mono-benzoyl derivative, from which he later produced a crystalline, epinephrine-hydrate, which he believed to be identical to the gland extract. It was this hydrate that Takamine further purified to provide "Adrenalin".

spelt with a capital “A” and without a terminal “e”, behaviour that brought a whiff of scandal to the pharmaceutical industry which was to last for many decades in America.³¹ But, by 1901, the word *adrenaline*, with a lower case “a” and with or without the terminal “e”, began to achieve widespread recognition in Britain as representing the active principle of the suprarenal gland.³² This was especially so amongst physiologists and, significantly, when Takamine presented a communication to the Physiological Society in that year, he spelled the word with a lower case “a” and made no reference to any commercial associations.³³ Takamine’s work stimulated much commercial and academic interest, including that of Wellcome, who wrote to Dowson of the WPRL, “[T]he suprarenal matter is exceedingly important and we ought not to be behind anybody”.³⁴

Thus, by 1906, *adrenalin* was the word that Henry Dale intended to use in his paper, but could he, as a member of staff of the Wellcome organization, a body with a fierce reputation for defending its own trade names, be allowed to use a word registered as a rival trademark?³⁵ Wellcome ruled that he could not, and turned down Dale’s request. The veto from Wellcome, and criticisms from the staff of the WCRL, first embarrassed, and then irritated, Dowson, who, as Director of the WPRL, had initially given Dale permission to use the term. He interpreted Wellcome’s censorship as criticism of his own authority, and explained in a lengthy submission to Wellcome that Dale had already published the disputed word without interference from the Company.³⁶ To substantiate his case, he sent Wellcome a quote from a current paper in the *Journal of Physiology*, illustrating the contemporary use of the word *adrenaline*,³⁷ and continued in his defence of the practice:

³¹ Many years later Dale recalled his first meeting, in 1909, with Abel, “[who] as he told me quite frankly when we met, had been rather suspicious of me; I was then working in the Wellcome laboratories, and he explained that he did not approve of pharmacological research with any sort of commercial connexion. Cushman, however, had persuaded him that I was not so bad as all that”, H H Dale, ‘Tribute from the British Pharmacological Society and personal reminiscences’, in *Tributes to John Jacob Abel from foreign societies*, Baltimore, Johns Hopkins University, 1957, pp. 5–12, 21–2, quote on p. 8. C Voegtlin, ‘John Jacob Abel, 1857–1938’, *J. Pharmacol.*, 1939, **67**:373–406, gives a detailed account of the relationship and connections between Abel and Takamine.

³² The subject index to the *Journal of Physiology* contains entries for 13 papers or abstracts with the word *adrenalin(e)* in the title, before Dale’s full paper, the subject of this article, which finally appeared in 1906 in vol. 34. The *British Medical Journal*, the *Lancet*, *Chemist and Druggist* and the *Pharmaceutical Journal* all used “*adrenalin*” or “*adrenaline*” in their indices.

³³ J Takamine, ‘The isolation of the active principle of the suprarenal gland’, *J. Physiol.*, 1901, **27**: xxix–xxx (communicated to the Society by O F F Grünbaum). Whether any pressure had been put on him to conform to British practice is not known. For details of Takamine’s career see F O Taylor, ‘Jokichi

Takamine’, in Dumas Malone (ed.), *Dictionary of American biography*, 20 vols, London, Humphrey Milford, 1936, vol. 18, pp. 275–6.

³⁴ Wellcome to Dowson, 19 Dec. 1901, TWFL:LB31, Letter/Memoranda Book 1901–1906, pp. 1–2. Dowson does not appear to have replied, or to have developed appropriate research work at the WPRL.

³⁵ Burroughs, Wellcome & Co. had only recently been involved in a highly-publicized court action to defend “*Tabloid*”, see Turner, op. cit., note 6 above, pp. 14–15, and James, op. cit., note 6 above, pp. 292–3, and ‘Legal intelligence, High Court of Justice, Chancery Division: the “*Tabloid*” case’, *Pharmaceut. J.*, 1903, **71**:925–7.

³⁶ Wellcome was abroad and Dowson’s letter was passed, according to standard practice, through the Company headquarters. Thus started the communication avalanche. The previous communication referred to is H H Dale, ‘The physiological effect of chrysotoxin’, *J. Physiol.*, 1905, **32**: lviii, and it must be inferred from the correspondence that Dowson had permitted the earlier use of the disputed word.

³⁷ J N Langley, ‘On the reaction of cells and of nerve endings to certain poisons, chiefly as regards the reaction of striated muscle to nicotine and to curare’, *J. Physiol.*, 1905, **33**: 374–413, especially p. 407.

Henry Dale and Adrenaline, 1906

[Dale] proposes to adopt the term “Adrenaline” the added “e” making the term indicate a basic substance conformably to the practice of chemists. The term thus spelled would take its place in scientific nomenclature and be descriptive both of its origin and character. I trust this has your consent; for although in papers published by the Chemical Society the substance is referred to as “epinephrine” the use of a term based on the descriptive name “adrenal” appears to be unavoidable in a physiological paper. The fact is that physiologists do not recognise the substance by any other name.³⁸

Wellcome was not impressed by Dowson’s rejoinder, and continued to insist that the physiologists should use the word epinephrine in line with the practice of staff from the chemical labs. At this point scientists from the WCRL, principally Dr Hooper Jowett, explicitly entered the debate, although it seems likely that they had been involved from the very beginning.³⁹

Hooper Jowett, Power’s deputy at the Chemical Laboratories, was a distinguished scientist with several published papers on epinephrine, and a recognized authority on its chemistry.⁴⁰ He and Power now tried to impose that authority on the physiologists, and argued strongly that the word epinephrine was scientifically correct. The fact that physiologists considered Abel’s epinephrine physiologically inactive was irrelevant. Jowett urged Dowson to comply with Wellcome’s wishes:

Bearing in mind the very strong reason that Mr. Wellcome has for the avoidance of the name ‘adrenalin’, I think we ought to do everything possible to carry out his wishes in this matter. As regards the Chemical Society, there is no difficulty about continuing to use the name ‘epinephrine’, as we have there a precedent to follow, and it is clearly indicated in my first paper what is meant by ‘epinephrine’. As regards other Societies and publications, I think that we could lay a very strong case before them for the use of this name ‘epinephrine’ . . .

[I]t seems to me that with the position the firm occupy and the scientific standing of the two Research Laboratories, it ought to be possible to convince any editor as to the reasonableness of our request to *continue* to use the name ‘epinephrine’ pointing out that we have done this since we published any work on this subject [his emphasis].⁴¹

Dale was quite unable to accept this viewpoint as he perceived an essential difference between the requirements of the physiologist and the chemist. He replied:

³⁸ Dowson to Wellcome, 2 Feb. 1906. The request did not receive Wellcome’s assent: see Wellcome’s comments on Dowson’s letter, 5 Feb. 1906; Pearson to Dowson, 8 Feb. 1906. All in TWFL: Acc 82/1: Box 23 ‘WPRL 1895–1922’. The authoritative *British pharmacopoeia* then available was a 1905 reprinting of the fourth edition published in 1898 and thus offered no guidance on the matter. By the time the fifth edition appeared in 1914 adrenaline, but not epinephrine, was listed, and no mention was made of any trade name associations. Martindale’s *Extra pharmacopoeia* of 1906 referred to “Adrenalin” as the active principle of the suprarenal gland, and listed several similar preparations, whilst the *British pharmacopoeia codex* of 1907 listed “adrenaline” and mentioned that adrenalin was a trade name.

³⁹ There is evidence of previous disagreements between Jowett and Dowson over the Company’s

suprarenal gland preparation (marketed as Hemisine) and its physiological standardization, with batches apparently being issued by the company without WPRL authority, see Dowson to Pearson, ‘The physiological assay of hemisine’, 18 Sept. 1905, WIHM:HSW ‘WPRL Material’. The physical proximity of the WCRL to the Company headquarters may account for the lack of written evidence of their earlier involvement.

⁴⁰ For example, H A D Jowett, ‘The constitution of epinephrine’, *J. Chem. Soc.*, 1904, 85:192–7; G Barger and H A D Jowett, ‘The synthesis of substances allied to epinephrine’, *ibid.*, 1905, 87:967–74. Unlike later work, in which Wellcome chemists and physiologists collaborated on joint investigations, Jowett’s papers never reported physiological data.

⁴¹ Jowett to Dowson, 20 Feb. 1906, WIHM:HSW.

In physiological literature the terminology is settled by those who describe the physiological action. Schäfer first described the action here in question and Langley first investigated it in detail. Neither these nor other physiologists owed anything to Abel's work or could make use of his inactive substances.⁴²

Further, Dale reminded Wellcome, physiologists were not particularly concerned with the chemical structure of the compound (a somewhat ironic comment from a man whose career did much to establish the relationship between physiological action and chemical structure), and he emphasized that the major, definitive physiological paper on the subject published in the *Journal of Physiology*, by T R Elliott, had been entitled 'The action of adrenalin'.⁴³ If he, Dale, now attempted to use the word epinephrine he would, by implication, be ignoring and discrediting the authority of physiologists whose work had made his own possible. Dale concluded that if the word adrenaline could not be employed, then the paper could not be published in the *Journal of Physiology*, and his position at the WPRL would be untenable. "[T]his I should most sincerely deplore, but the result would be inevitable".⁴⁴ To support his position Dale enclosed an authoritative statement by the Editor of the *Journal of Physiology*, J N Langley,

adrenalin is now the scientific name, & has become so rooted that it is futile to try & make scientific people go back on this & adopt instead a name which has been used & failed.⁴⁵

This had immediate effect. Wellcome promptly acknowledged that these arguments altered his viewpoint, and he accepted that the use of "adrenaline" in physiological publications was unavoidable. Although Dale's hint at resignation indicated, "a lack of mutual confidence and respect", he approved the paper, hoping, nevertheless, that Dale would distinguish the active chemical from the product of a rival company.⁴⁶

Thus the matter appeared to be settled. But the sanction was short-lived: less than twenty-four hours later Wellcome cabled Dowson forbidding the paper to be submitted for publication, and the next day a long letter arrived at the WPRL, explaining why he had withdrawn his permission to use the word adrenaline.⁴⁷ What changed his mind so precipitately? It was a copy of a letter from Jowett, originally sent to Dowson, pushing further the chemists' argument for epinephrine.⁴⁸ Jowett alluded to the legal problems that

⁴² Dale to Wellcome, 20 Feb. 1906, WIHM:HSW. The word adrenaline also achieved widespread general usage in continental Europe, see S Fraenkel, *Die Arzneimittel-Synthese auf Grundlage der Beziehungen zwischen chemischen Aufbau und Wirkung*, Julius Springer, Berlin, 1906, pp. 424–5. The copy in the Wellcome Institute Library originally belonged to the WPRL.

⁴³ Dale and Elliott collaborated closely in their complementary experimental work, and performed joint experiments at the WPRL and in Cambridge. Elliott's paper contains a specific acknowledgement to Dowson and the WPRL for the provision of facilities, see T R Elliott, 'The action of adrenalin', *J. Physiol.*, 1905, 32:401–67, especially p. 411.

⁴⁴ Dale to Wellcome, 22 Feb. 1906, WIHM:HSW.

⁴⁵ The series of letters that resulted in this statement are: Langley to Dale, 15 Feb. 1906; Dale to Langley, 16 Feb. 1906; Dowson to Pearson, 16

Feb. 1906; Dowson to Pearson, 18 Feb. 1906. All letters in WIHM:HSW. However, even two years later, another eminent physiologist, Edward Schäfer suggested the word "adrenine" to obviate the commercial associations of "adrenaline" and the chemical confusions of "epinephrine", see E A Schäfer, 'Oliver–Sharpey lectures on the present condition of our knowledge regarding the functions of the suprarenal capsules', *Br. med. J.*, 1908, i:1277–81, 1346–51, especially p. 1281.

⁴⁶ Wellcome to Dowson, 25 Feb. 1906, Wellcome to Dale, 25 Feb. 1906, both letters in WIHM:HSW. Annotated carbon copies of both in TWFL:Acc 82/1: Box 23 'WPRL 1895–1922'.

⁴⁷ Telegram, Wellcome to Dowson, 27 Feb. 1906, letter, Wellcome to Dowson, 27 Feb. 1906, both in WIHM:HSW.

⁴⁸ Jowett to Dowson, 20 Feb. 1906, sent by Dowson to Wellcome, WIHM:HSW.

might arise if Dale used the rival trade name and, with an eye to his own position at the WCRL, suggested that it was time to correct the erroneous use of “adrenaline” in physiological literature, and to ensure conformity in all publications coming from the Wellcome laboratories. Wellcome’s considerable respect for Jowett’s reputation and authority ensured that the latter’s comments carried much weight, especially as they reinforced concerns about the legal position. Wellcome’s long reply to Dowson and Dale, although acknowledging that the word was a “scientific descriptive term”, raised, yet again, the legal problems if they infringed another company’s trade name. He called on the physiologists to find “the moral courage” to correct their misuse of the word adrenaline, emphasizing, with more than a hint of a crusade:

Surely we are not so lacking in our resources or in our spirit of research that we cannot find some solution fair and just to all concerned. Why should we be faint-hearted? Our whole career has been strewn with difficulties and our successes largely incited by them. We certainly have not exhausted ourselves in this very limited discussion . . .⁴⁹

He put forward the practical proposal that all the interested parties, including representatives from the Physiological and Chemical Laboratories, and Company headquarters, should get together, motivated by

[T]he earnest desire we all have to hasten the publication of the ergot work which means professional interest to the WPRL and business interests to the firm.⁵⁰

He further suggested consultation with Professor Langley from Cambridge, and Dr Alfred Chune Fletcher,⁵¹ whom he considered

one of the ablest medico-legal experts in the Kingdom. His judgements I find as wise when they are against me as when they are in my favour. In his wisdom I feel confident you will gain some help.⁵²

Dowson and Dale responded immediately to this set-back, although from different standpoints. By this stage, five weeks into the discussions, Dowson focused on his own authority and position as the independent Director of the WPRL. He stressed that he had received Wellcome’s authorization with relief, especially as it would guarantee the future “moral support” of the Cambridge Physiological School, and expressed his indignation at what he now interpreted as unwarranted interference from members of the WCRL and from Wellcome himself. He reminded Wellcome

If there is one subject more difficult to handle than another in scientific laboratories owned by the principal of a commercial firm it is the publication of work; and the degree of restriction under which this is done affords a sure test of the scientific status of such laboratories. To take care that

⁴⁹ Wellcome to Dowson, 27 Feb. 1906, WIHM:HSW.

⁵⁰ Ibid.

⁵¹ Chune Fletcher was a close friend and adviser of Wellcome, frequently consulted on matters of medical “etiquette” and ethics, such as the problems of achieving Home Office registration for the WPRL. Dale, in later life, commented to T R Elliott, “I suppose that Alfred Chune Fletcher, the Medical Officer to the Charterhouse . . . knew him [Wellcome] better than anybody else did. Fletcher

and Wellcome used fairly often to go off for weekends together, but Fletcher was too discreet, and too loyal to talk about the extraordinary and paradoxical mixture of characteristics in Wellcome . . . [He was] my very good friend and adviser in my early days of service and dispute with Wellcome”, 6 June 1958, Royal Society Archives, Sir Henry Dale papers, 93HD 36.4.29 ‘T R Elliott’. See also WIHM:HSW papers on Chune Fletcher.

⁵² Wellcome to Dowson, 27 Feb. 1906, WIHM:HSW.

no restrictions arising purely out of commercial considerations should hamper the workers here is at once the most delicate and responsible task of the director; and yet, under a misapprehension of the ethics of the epinephrin position, you appear to be bent on exercising a power of veto which to your director appears to be unjustifiable. The final adjudication on the question which has arisen is the one thing which you should leave to me after assuring yourself that I have not overlooked any important considerations.⁵³

Dowson concluded his trenchant remarks with further objections to Jowett's continuing involvement and grudging acceptance of Chune Fletcher as a "referee" in the debate.

Dale's response to Wellcome was equally uncompromising, and scathingly critical of Jowett's opinions, "Dr. Jowett's convictions are interesting; they may even be true: but they are entirely beside the point".⁵⁴ But, exhibiting an early flair for the diplomatic and political activities that were to become major responsibilities in his later life, Dale had made an important connection that Dowson had not—he had been to talk to Chune Fletcher.⁵⁵ Dale was thus confident, when writing to Wellcome, of the nature of Chune Fletcher's recommendations. He was careful to address only the problems of scientific importance, and made no mention of the issues of authority and interference that so agitated Dowson. Dale emphasized yet again that the chemical called epinephrine, isolated by Abel and used by chemists, was not physiologically identical to the crude gland extract, although he recognized, and sympathized with, the difficulties raised by the episode. He added a powerful coda:

The position is one of far more difficulty than you, probably, can conceive. There is among English medical men and particularly among physiologists, a strongly marked prejudice against any connection with commerce. That prejudice I am earnestly and constantly trying to break down on my own behalf, and on that of any pharmacological workers in your laboratories. I have great hope of success: but the position I am striving for, on your behalf as well as my own, would be seriously imperilled by a breath of suspicion that the publication of my work was hampered or modified by other than scientific considerations.⁵⁶

Those arguments were well targeted. Simultaneously Chune Fletcher, after interviewing all the participants in the debate, reported to Mr Pearson, who relayed the opinion to Wellcome:

Mr C.F. [Chune Fletcher] tells me that his opinion of the matter is that Dr. J. [Jowett] is right from a *chemical* point of view & Dr. Da [Dale] is right from a *physiological* point of view, *and as a physiologist he cannot describe the substance with which he has been working as 'Epinephrine'*—the substance Dr Da has been working with is known to physiologists as 'adrenaline' [underlined in red in the original].⁵⁷

⁵³ Dowson to Wellcome, 5 March 1906, WIHM:HSW. A copy of this, in TWFL: Acc 82/1: Box 23 'WPRL 1895–1922', was received by Henry Wellcome, and the lengthy passage quoted is underlined and annotated by him.

⁵⁴ Dale to Wellcome, 6 March 1906, TWFL: Acc 82/1: Box 12.

⁵⁵ See note 57 below.

⁵⁶ There are two extant copies of this letter, Dale to Wellcome, 6 March 1906: the carbon copy from the Company files is in WIHM:HSW; the original,

heavily annotated by Wellcome, is in TWFL: Acc 82/1: Box 12.

⁵⁷ Report of Chune Fletcher's opinion, by Pearson to Wellcome, undated, but c. early March 1906, TWFL: Acc 82/1: Box 23 'WPRL 1895–1922'. These notes also make it apparent that Dale had independently consulted Chune Fletcher before the latter's formal involvement in the affair, and that his controversial letter cited in note 44 above, in which resignation had been obliquely indicated, had been written on Fletcher's advice.

Faced with this barrage Wellcome finally agreed, on 8 March, that, subject to the inclusion of an explanatory footnote differentiating the preparations used, Dale could submit his paper.⁵⁸ Having learned from the previous short-lived dispensation, Dale immediately despatched his manuscript to the *Journal of Physiology* in Cambridge, diplomatically but purposively, writing to Wellcome:

I hope that the vigour with which I have urged the difficulties in the way of changing the attitudes of the physiological world has not given you the impression that I viewed at all lightly the difficulties of the commercial position.⁵⁹

Thus ended Dale's direct involvement in an incident that had been enormously worrying: his wife was expecting their second child, and his employment prospects, should resignation have been necessary, looked bleak. Despite Wellcome's decision, Jowett continued his campaign for the sole use of epinephrine for some months, a campaign to which the staff of the WPRL remained completely unresponsive.⁶⁰

The Significance of the Debates

These debates are instructive at several levels, including the legal, the scientific and the personal. Whatever the precise legal situation that prevailed at the time, the discussions about the propriety of infringing another company's rights, and indeed the relevance of ethical pharmaceutical advertising to the proper conduct of medical research were at the heart of the dilemma facing Wellcome. There is only a hint in correspondence between Henry Wellcome and the Managing Director of the Burroughs, Wellcome Company, that Parke, Davis & Co. had threatened legal action in 1906, and no confirmation of this has been found in other records relating to the labs or to the Company.⁶¹ Neither can I find strong evidence that adrenaline was a registered trade name for Parke, Davis & Co., in Britain at that time. Many years later, when challenged about the incident by an American pharmacologist, Henry Dale admitted:

Investigation showed, however, that they [Parke, Davis & Co.] had no trademark for the name in this country, and they had in fact, never had one. I do not pretend to know the reason as to why they

⁵⁸ Wellcome sent formal copies of his permission ("Dear Sir", rather than the usual "Dear Dr. Dowson") to the WPRL and to Mr Pearson of the Company. Several further items of correspondence, querying and then confirming the precise wording of the footnote, all dated between 8 and 10 March 1906, are in WIHM:HSW. The published footnote reads, "In accordance with physiological custom the name 'adrenaline' is used throughout this paper to denote the active principle of the supra-renal gland, in whatever form administered. Simple extracts of the gland, commercial preparations issued under various 'brand' names, and solutions of the pure base, without preservative, were all used, and all give the effects described", H H Dale, 'On some physiological actions of ergot', *J. Physiol.*, 1906, 34:163–206, quote on p. 169.

⁵⁹ Dale to Wellcome, 14 March 1906, TWFL:Acc 82/1:Box 23 'WPRL 1895–1922'.

⁶⁰ Differences between academic and commercial concerns continued however: for example, the British

chemist H D Dakin, working in 1906, wrote, "A considerable part of my work has, however, been anticipated by workers in the laboratory of Meister, Lucius & Bruning . . . I take the opportunity of stating that my results were entirely independently arrived at, and that owing to the method of publication adopted (Patent Specifications), it is only recently that I have become acquainted with the main portion of their work", see H D Dakin, 'The synthesis of a substance allied to adrenalin', *Proc. R. Soc. Lond. B.*, 76: 491–7, quote on p. 491.

⁶¹ The hint is in confidential Company correspondence, but no confirmation has been located, Wellcome to B W & Co. [n.d. but between 3 and 7 March 1906] TWFL:LB32 Letter Book, April 1905 to March 1906, p.78. However Parke, Davis & Co had proved litigious in other countries, see, e.g., *Chemist and Druggist*, 1904, 64:377, 934; 65:22, 495, 547.

did not obtain registration. There is, however, one salutary item in the English law on the subject, which may have had something to do with it. The English law recognises the trademark only as indicating the preparation of a particular firm, and, if the owner of the trademark allows it to pass into currency as the general name of the substance, apart from his particular manufacture, he loses all rights in the trademark, and it is removed from the Register. I do not think that the American law is as strong on this point. In any case it has suited Parke Davis's purpose, I think, to allow the name 'adrenaline' to be freely used in English scientific literature, and at the same time keep tight hold of their trademark rights in the United States.⁶²

So were Henry Wellcome and his advisers being extra cautious in trying to head off a threat before it appeared, or was even known to exist? Or did the Wellcome chemists use the possibility of a legal problem as a cover, or a threat, to try to force the physiologists into line with *their* normal practice?

That leads to a second feature of the debates—the professional relationship between the chemists and the physiologists employed by Wellcome. At first glance the whole disagreement might be interpreted as a fundamental scientific difference—on the one hand, a compound that the chemists had abstracted from the adrenal glands and named epinephrine, and, on the other hand, an argument from physiologists that epinephrine was not physiologically identical to gland extracts in their tests and that another word was necessary for the active material. From Takamine's chemical work this active material was known to be the substance called adrenalin. There thus seems to be little scientific reason for the chemists to have become heavily involved in the discussions, as the immediate problem was not one of scientific terminology but of the possible infringement, and subsequent liabilities, of Parke, Davis' rights. By suggesting that *a* solution, indeed *the* solution, to the problem was the imposition of an unsuitable word, the chemists added confusion and fostered resentment.

The history of the word "epinephrine", as originally proposed by Abel and Crawford in 1897, is chequered. The following year, Abel acknowledged that his extraction method was not yet perfected, "[I]n its native state, as found in the suprarenal capsule, this substance differs by one chemical reaction only from its state as described in this paper."⁶³ Abel's further chemical work continued to refine his extraction procedures. The difficulties imposed by the continuing use of the word epinephrine for his extracts during this on-going process, led him to concede:

At the present moment it is impossible to express in analytical terms, the differences that exist between the epinephrine of my former papers and the somewhat less altered native principle.⁶⁴

⁶² Dale to Leake, 15 Oct. 1935, RS 93 HD. 39.25.4. Dale may well have been correct in believing that Parke, Davis gained from allowing free use of the word in England. The details of this debate emphasize that historically "epinephrine" and "adrenaline" are not the same substance, although they are now considered to be so. E E J Marler (compiler), *Pharmacological and chemical synonyms: a collection of names of drugs and other compounds drawn from the medical literature of the world*, Amsterdam, Excerpta Medica, 1973, pp.

173–4, lists a further 57 synonyms, including "takamina".

⁶³ J J Abel, 'Further observations on the chemical nature of the active principal of the suprarenal capsule', *Johns Hopkins Hosp. Bull.*, 1898, 9:215–18, quote on p.218. Abel's own research depended on the generosity of Messrs P D Armour & Co. of Chicago and the assistance of G A Manns, the company's chief chemist.

⁶⁴ J J Abel, 'Further observations on epinephrin', *Johns Hopkins Hosp. Bull.*, 1901, 12:80–4, quote on p. 84.

And just a few months later he presented a detailed comparison of a series of epinephrine compounds with Takamine's adrenalin, and von Fürth's "suprarenin". Hampered by Takamine's failure to describe his methods or to provide adequate analytical data, Abel suggested that adrenalin, which he admitted was more physiologically active than epinephrine, was in fact a mixture and not an individual substance.⁶⁵

These detailed arguments continued for some time and are beyond the scope of the present paper. They do, however, show the importance of the point made by Henry Dale in his campaign, that there were significant and relevant physiological differences between the variously named chemicals.⁶⁶ From the correspondence and other papers examined in this case-study, it appears however that these empirical scientific arguments about chemical and physiological nomenclature were not seriously considered within the company, despite the efforts of some of the proponents, especially Dale and Jowett.

What is clear, is that personal differences between Jowett and Dowson coloured their responses. Confidential notes made at the time by Wellcome on some of the personalities are immensely revealing. His opinion of Dale reads,

Dr Dale is a very able man and has will and a way of his own that needs very diplomatic handling & he has *very strong ideas* about professional ethics and, I think he probably knows & has thought more about this side which it is necessary for us to keep in view—I am sure Dr Dale will not *intentionally* do anything not strictly loyal . . . I consider him the best man in his work I have ever met—for a young man, and he is developing well & I want him to develop my ideals in this Physiological work—in which we are far ahead of others.⁶⁷

His view of Dowson was far less flattering, and underlines how the conflict of personalities influenced the nomenclature debate,

I am afraid that Dr D[owson] is and has been throughout this discussion in one of his 'moods'. . . . I fear that he personally far more than Da[le] is responsible for the present situation . . . Dr D[owson] lacks tactfulness and as we know by past experience when he is in his 'moods', stirs up & fosters discord and suggests bad motives and uses regrettable expressions—I am deeply sorry that he has got his knife into Jow[ett]. . . . I am afraid from the tone of the correspondence that Dr. D[owson]

⁶⁵ For example, J J Abel, 'On the behaviour of epinephrine to Fehling's solution and other characteristics of this substance', *Johns Hopkins Hosp. Bull.*, 1901, 12:337–43, especially, 'Comparison of epinephrin with the substances known as suprarenin [*sic*] and adrenalin', pp. 34–2; *idem*, 'On a simple method of preparing epinephrin and its compounds', *ibid.*, 1902, 13:29–36; *idem*, 'On epinephrin and its compounds, with especial reference to epinephrin hydrate', *Am. J. Pharm.*, 1903, 75:301–25. The later discovery, that the medulla of the adrenal gland contains both adrenaline and non-adrenaline, the latter being more physiologically active, provides an additional explanation for the chemical and physiological confusion, see, e.g., Ulf S von Euler, *Noradrenaline: chemistry, physiology, pharmacology and clinical aspects*, Springfield, Ill., Charles C Thomas, 1956, especially pp. 109–16. Abel, in later life, commented that epinephrine was "the name coined by me thirty years ago at a time when I supposed that the form in

which I had succeeded in isolating it represented the base as it actually exists in the capsules", and acknowledged that the confusion and competing claims at the time meant that "I can not look back on my own poor efforts to elucidate the chemical constitution of the compound with pleasure", in J J Abel, *Chemistry in relation to biology and medicine with especial reference to insulin and other hormones*, The Willard Gibbs Lecture, Baltimore, Williams & Wilkins, 1939, especially pp. 60–7.

⁶⁶ This was also emphasized by Parke, Davis & Co., see for example their letter, 'The pharmacology of the suprarenal gland', *Pharmaceut. J.*, 1903, 71:870.

⁶⁷ Consecutive undated notes, Wellcome to BW & Co, c. Feb. 1906, TWFL:LB32 Letter Book, Feb.–April 1906, p.25, emphasis as in the original. Wellcome's recognition of his ability led him to appoint Dale as Director of the WPRL later in 1906 when Dowson resigned for reasons unconnected with the present incident.

made up his mind early and then as he too frequently does closed his doors to conviction and regarded anyone who differed from him as wrong. This with Dr. D[owson] is a matter of temperament for temperament governs his moods & methods.⁶⁸

Thus Dowson's temperament, and the threat of legal action, real, imagined, or deliberately manufactured, contributed greatly to the escalation and maintenance of the dispute. Equally important was the question of scientific authority, both within the Wellcome organization and, more critically, in wider medical and scientific circles. Some of the tensions between the Physiological and Chemical labs were engendered by the fact that the staff of the WCRL wished to control those they clearly regarded as their junior colleagues. But, more significantly, this controversy and its resolution illustrated the personal aspirations of Henry Wellcome to achieve scientific respectability, and acceptability, for his laboratories. From its establishment, Burroughs, Wellcome & Co. used scientific language and symbolism to advertise their products, and to promote themselves as advanced, responsible pharmacists. The creation of apparently independent laboratories, run on high-minded scientific principles untainted by commercial considerations, further enhanced and extended that representation. That image was projected very successfully to pharmacists, general medical practitioners and other pharmaceutical manufacturers. However, as Wellcome discovered when he tried to register the WPRL for animal experimentation, that claim had not impressed either the senior medical establishment or government officials, who viewed the Company and its laboratories not as scientists, but as mere commercial tradesmen who could not be accorded the rights and privileges given to men of medical and scientific standing.⁶⁹ Wellcome's eventual success at getting his laboratories registered under the 1876 Cruelty to Animals Act was a considerable achievement. Thus, challenged about the scientific independence of the labs, when the question of using the word adrenaline arose, Wellcome was torn between commercial propriety and scientific credibility. He showed himself particularly sensitive to the advice of J N Langley, and heeded the caution of Dale and Chune Fletcher that an imprudent decision imposed on the physiological laboratories would do irreparable harm to his schemes and ambitions. Ultimately, the claims for scientific reputation and independence won.⁷⁰

In a letter to Wellcome during the dispute, Dale had spelled out very clearly the difficulties of pursuing scientific research in an establishment associated with a commercial firm. He promised Wellcome that he would discuss, with Frederick Gowland Hopkins, the Chairman of a Physiological Society committee on proteid nomenclature, the possibility of extending that committee's terms of reference to include the problems of using commercial preparations.⁷¹ His final paragraph summarizes the novel problems that

⁶⁸ *Ibid.*

⁶⁹ The debates on the animal experimentation issue and their resolutions are documented in Tansey, *op. cit.*, note 5 above.

⁷⁰ The adrenaline/Adrenalin debate was much easier for Wellcome to be accommodating on, than say, allowing publication of a paper that reflected negatively on a company product. The WPRL's stance on openly publishing commercially profitable and patentable procedures was questioned during the

earlier campaigns for Home Office registration, see Tansey, *op. cit.*, note 5 above, pp. 28–9.

⁷¹ Dale to Wellcome, 14 March 1906, TWFL:Acc 82/1:Box 23 'WPRL 1895–1922'. An annotated copy [by Wellcome?] is in WIHM:HSW. Dale admitted, "I confess, however, that I have no great hope in the matter", and I have been unable to find evidence that the Proteid Nomenclature Committee did consider commercial preparations.

faced the Physiological Research laboratories, encapsulated, and in this instance resolved, in the dispute about the use of the word adrenaline.

The question is at bottom a practical one. The connection between chemistry and commerce is an old and honourable one: that of physiology is a new thing to England, and regarded with jealousy and suspicion by the 'professionally correct' medical and physiological people. You may not know that my predecessor Dr Shaw was blackballed by the Physiological Society merely on the grounds of his supposed connection with commercial interests. The situation needs delicate handling, and I am sure I may rely on you for any possible concession to old-fashioned prejudice, provided that it is compatible with dignified independence and due regard to your firm's interests. You will see how difficult it is for me to press a matter of this kind when there are people always ready to detect a commercial manoeuvre in the policy of these laboratories. But I am going to do what I can: and I hope some day to see the aid of commerce by physiology recognised as an important and desirable branch of medical science in England, and to see your laboratories recognised as the pioneer institution.⁷²

Recalling the incident in his Personal Record at the Royal Society, Henry Dale commented over fifty years later,

I am not nearly so sure now, as I was then, that I was completely justified to the merits of the case. I am very sure however, that I won an important victory for the staff of the Laboratories.⁷³

At a personal level, the adrenaline episode was of considerable significance in Dale's maturation as a scientist and scientific tactician, representing the first of many episodes in his career associated with the correct use of pharmacological terminology. His personal research work attracted attention from pharmacologists at home and abroad, as exemplified by a particularly pertinent comment from the British pharmacologist, A R Cushny, writing to J J Abel in 1909.

There is a very good man H. H. Dale here, who has done well with ergotoxin and is I think one of the most promising men about. The difficulty is that he is pharmacologist to Burroughs and Welcome [*sic*], and though that does not affect his work, you might not wish to make a precedent. He is not at all concerned in pushing the products of the firm however, and simply works in his laboratory.⁷⁴

⁷² Dale to Wellcome, *ibid.* A careful examination of the Candidates Books of the Physiological Society has failed to reveal confirmation of Dale's assertions about Vernon Shaw. Shaw was elected to the Society in 1904, without apparent opposition or undue delay, Physiological Society Archives, Contemporary Medical Archives Centre (CMAC), SA/PHY/E.2/3, see also, 'W.V. Shaw, OBE', *Nature*, 1937, 1:359. The attitude of the American Society for Pharmacology and Experimental Therapeutics was much harsher: they forbade membership to anyone associated with a pharmaceutical company, see J Parascandola, 'The "Preposterous Provision": The American Society for Pharmacology and Experimental Therapeutics' ban on industrial pharmacologists, 1908–1941', in J Liebenau, G J Higby, and E Stroud (eds), *op. cit.*, note 12 above, pp. 29–47.

⁷³ Feldberg, *op. cit.*, note 2 above, quote on p. 98.

⁷⁴ Cushny to Abel, 22 Feb. 1909, A R Cushny papers CMAC/PP/ARC/D.1. Abel had requested advice on inviting a British pharmacologist to join the editorial board of the *Journal of Pharmacology*. Cushny's reply indicates yet again some of the prejudices extant about the association of scientists with pharmaceutical companies. For further details of Abel's attitude towards pharmaceutical companies see Parascandola, *J. J. Abel*, *op. cit.*, note 29 above, especially, 'The bias against industrial pharmacologists', pp. 115–25; *idem*, *op. cit.*, note 28 above. See also note 31 above. For a wider American perspective see J P Swann, *Academic scientists and the pharmaceutical industry: cooperative research in twentieth-century America*, Baltimore, Johns Hopkins University Press, 1988, especially ch.2, 'The rise of university-industry interactions in biomedical research'.

In 1913, still employed by Wellcome, he was appointed an official adviser to the *British pharmacopoeia*; during the First World War he provided advice and technical expertise to British manufacturers attempting to replace suspended German patents; after that war the creation and proper identification of national and international biological standards were major official concerns of Dale; and in his research work his ability to distinguish, classify and name drug effects made enormous contributions to the development of work on the chemistry of the nervous system.⁷⁵

The resolution of the adrenaline debate was pivotal in emphasizing the independent scientific autonomy of the WPRL and its staff, as Wellcome had so frequently proclaimed, somewhat inaccurately, in the past. It also established a base for scientific excellence that distinguished research associated with the Wellcome organization for many decades.⁷⁶ The fostering of scientific research in the environment of a pharmaceutical company had created novel problems. Nevertheless, by addressing such unforeseen difficulties, the Wellcome company managed to develop policies to accommodate pure scientific work alongside commercial interests, policies that were later emulated by other companies.⁷⁷

⁷⁵ For further details of Dale's career, see Feldberg, *op. cit.*, note 2 above, and Tansey, *op. cit.*, note 2 above. His important contributions to pharmacological terminology include "sympathomimetic", "adrenergic", and "cholinergic", see, e.g., H H Dale, 'Nomenclature of fibres in the autonomic system and their effects', *J. Physiol.*, 1934, **80**: 10P.

⁷⁶ In 1914 Dale became the first elected Fellow of the Royal Society associated with a pharmaceutical

company, and several of his colleagues achieved the same distinction, see Tansey, *op. cit.*, note 5 above, pp. 36–7. In 1936, then an employee of the Medical Research Council, Dale was awarded a Nobel Prize, the first of five scientists associated with the Wellcome Laboratories to be thus honoured so far.

⁷⁷ Such debates and dissensions continue to the present day however, see the contemporary debate about the word "Taxol", and the activities of Bristol-Myers Squibb, e.g., *Nature*, 1995, **373**:370.