General and Comparative Endocrinology 280 (2019) 43–46

Contents lists available at ScienceDirect

General and Comparative Endocrinology

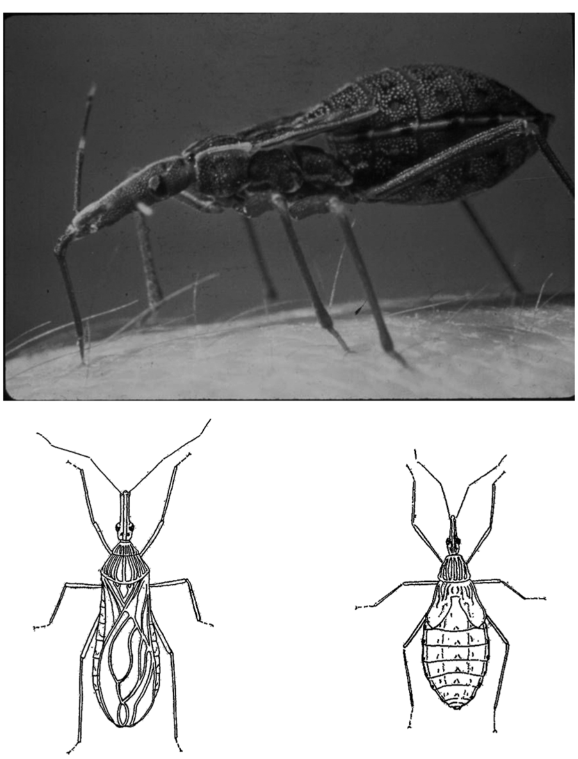
journal homepage: www.elsevier.com/locate/ygcen

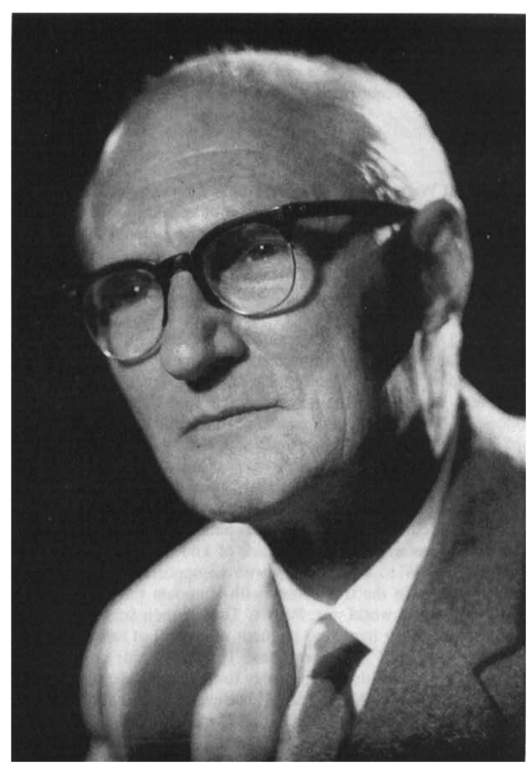
In Memoriam

PROFESSOR SIR VINCENT B. WIGGLESWORTH, C.B.E., M.D., F.R.S. (1899–1994) 25 YEARS ON: HIS LEGACY AND LESSONS FOR MODERN TIMES

It is an honour to write this tribute to the founder of two major biological disciplines at 25 years from his passing. I hope to illustrate that his incisive mind and prodigious publications are of far more than historical interest; they are the product of a mind that created many conceptual foundations in physiology which provide valuable guides to clear scientific thought and actions, which are as relevant today as they were a century ago. He fathered both Neuroendocrinology and Insect Physiology. He wrote 266 papers and 10 books over 70 years (listed by Gupta (1990)). Such huge achievements are not the mysterious products of a superior intellect or consummate hard work alone. They resulted from a penetrating clarity of mind that flourished in relative solitude, which enabled him to identify, and focus on, scientific problems that represented the issues of core importance to a discipline, leaving the details to be filled in later, or by others. A mere 18 of his publications have co-authors. His adult life embraced a love of his work, commitment, perseverance and a good dose of serendipity. He taught us all by example that crucial lesson in science: you must enjoy it to have the intense motivation needed to do it, which remains valid for us all.

Sir Vincent B. Wigglesworth (VBW to all who knew him well) became fascinated with the life of insects as a young child, but was despatched at the age of seven to two tough, traditional English boarding schools and then joined the Royal Field Artillery in 1917. His unit was moved to the front line in France just after the signing of the Armistice. Michael Locke (1996) insightfully concluded that these experiences "left him with an almost impermeable shell through which he found it difficult to show emotion, contributing to the sense of remoteness that





The fifth instar *Rhodnius* feeding on a student's arm is only one third full; it imbibes its own body weight in blood each minute for about 10 minutes, the abdomen becomes roughly spherical and the legs barely reach the ground. The distension initiates release of an avalanche of hormones.

https://doi.org/10.1016/j.ygcen.2019.04.009
Received 25 December 2018; Received in revised form 5 April 2019; Accepted 7 April 2019
Available online 11 April 2019
0016-6480

he conveyed to colleagues". But those who saw through that shell, found within a warm and gentle man with a wry humour and warm heart. He went up to Gonville and Caius College, Cambridge, in 1919 and completed an M.D at St. Thomas' Hospital in London, where he published papers on mammalian intermediary metabolism, mostly with J.B.S. Haldane. This work fostered in VBW a growing belief that the central problems of animal physiology could not be solved in complex, higher vertebrates, but required systems with fewer and more accessible cells, such as he recalled viewing through his child's microscope in insects. And it was well known that insects survived surgical atrocities that it would be unacceptable to attempt on higher animals.

The first catalytic change came in 1926, when Patrick Buxton offered VBW a lectureship in medical entomology at the London School of Hygiene and Tropical Medicine (LSHTM). Buxton discussed with VBW how medical entomology was in dire need of order in its scattered literature, which both men agreed would be best remedied by undertaking a significant piece of research in each main area of physiology, using a diversity of insects of VBW's choice. There ensued a flood of publications from LSHTM on various species, mostly assembled into his monograph 'Insect Physiology' (Wigglesworth, 1934a), modestly proclaiming this new field. In the course of these varied studies, it became clear to both Buxton and VBW that certain insects were more amenable than others to particular experiments. Buxton introduced VBW to *Rhodnius prolixus* (Hemiptera, Reduviidae) (hereafter, *Rhodnius*) a blood feeding bug with unique attributes. A single large blood meal would unleash its progressive growth and development (moulting) into the next instar with "clock-like accuracy" (Beament, 1994) and it would not feed again until after ecdysis; it then entered a developmental arrest (but remained physically active) until given another blood meal, which initiated its development to the next instar. In other animals, continued feeding is essential for continued development, such that attempts to study one process led to interference with the other, thereby confounding both. But in *Rhodnius* it seemed possible to study development and feeding independently. Moreover, the interval between blood feeding and ecdysis was unusually long (c. 21 days) enabling precise pinpointing of all the physiological changes during development with extreme precision. Buxton published the biology of *Rhodnius* in 1930, with much of the data in it provided by VBW, and the study of growth and development suddenly became vastly more accessible. VBW eventually published 65 papers specifically on *Rhodnius* (see Locke (1992)), which became affectionately known as 'VBW's bug'. *Rhodnius* remains a favourite model in which to study all phenomena related to insect growth and development and many other topics (see Locke (1992)). Current students faithfully post VBW's timetables for rearing *Rhodnius* (from Buxton (1930)) on their laboratory walls. At 2018, the Web of Science lists 1433 papers with '*Rhodnius prolixus*' in the title, and a stable average of 33 papers per year over the past decade. Google Scholar finds 26,500 papers that mention *Rhodnius prolixus*. The utility of 'VBW's bug' has certainly not diminished!

VBW's early papers on *Rhodnius* were seminal (Wigglesworth, 1933, 1934b). He used ingeniously simple decapitation and parabiosis experiments of insects from different instars to show that the head was the source of a hormone that controlled moulting. At that time, only glands were accepted as sources of hormones, while the Nerve cells communicated only electrically. This dogma led VBW to assume initially that the source of his 'moulting hormone' must be a gland in the head; only one was known, the corpus allatum (Nabert, 1913), but he was unable to confirm that the corpus allatum was the source of the hormone. He noted (Wigglesworth, 1985) that while writing up his results, Julian Huxley informed him of the work of Kopeć (1922) on the gypsy moth caterpillar, in which the brain was proposed as the source of an equivalent hormone. However, Kopeć's findings had already been hotly rejected, for two reasons. First, Kopeć seemed unaware that his proposal was immensely controversial, and he did not defend it. Second, his claim that surgical removal of the brain inhibited pupation of the caterpillars was attributed to their starvation, caused by the inability of operated caterpillars to continue to feed. Kopeć's own data showed that they died desiccated and shrivelled. This was precisely the type of problem for which Buxton and VBW saw *Rhodnius* as the solution! Indeed, headless *Rhodnius* learned to walk again and frequently outlived intact bugs by months. Thus, VBW's work (1934b, 1936) cast doubt on the accepted dogma that the nervous system did not produce hormones, in ways that Kopeć's work did not. Earlier studies (Speidel, 1919, Favaro, 1925) had described apparently 'secretory droplets' in caudal spinal nerves of fish, which were derided by endocrinologists as pathological features. Following a lecture by VBW on his 'head hormone' in Copenhagen in 1936, Bertil Hanström discussed with him the finding by Otto Pflugfelder (1936) of very similar secretory material in the brains of several other bugs, and encouraged VBW to send him fixed brains of *Rhodnius*. Hanström found such cells in the dorsal protocerebrum of *Rhodnius* (Hanström, 1938). VBW promptly excised this region of the brain from moulting *Rhodnius* and implanted it into headless host *Rhodnius* that are normally unable to moult, thereby causing them to moult (Wigglesworth, 1940). This was the first demonstration of a functional neurohormone in any animal, and thereby constituted the birth of Neuroendocrinology. To this day, reviews of insect endocrinology continue to cite Kopeć as the first proof of this phenomenon in insects. VBW then showed that the corpus allatum secreted a different hormone, the juvenile hormone, which restrained development of adult features during moulting, but did not cause it (Wigglesworth, 1936, 1940, 1948). His 'brain hormone' was then found to induce moulting indirectly by promoting secretion of a steroid hormone from glands in the prothorax (Wigglesworth, 1952). Thus, an entire endocrine regulatory complex of three hormones was revealed within a few years.

Of VBW's prodigious output, these few papers are his most memorable, catalytic and highly cited, as they simultaneously created two new disciplines and mapped out for readers the pathways by which to discover their intricacies. In 1936, VBW was promoted to Reader, elected to Fellowship in the Royal Society (F.R.S.). In 1939, he published the first of seven English editions of 'The Principles of Insect Physiology' (Wigglesworth, 1939–1972), cementing his status as 'the father of insect physiology'. Successive Prefaces to each edition attest to the explosive growth of the fields he unleashed. In 1939 he noted simply that "insects provide an ideal medium in which to study all the problems of physiology", whereas by 1965 the field had become so vast "that to master the advances that are being made on so many fronts… is becoming beyond the range of a single author".

The second catalytic change came in 1943. He was appointed by the Agricultural Research Council (ARC) to be Director of a new ARC unit of Insect Physiology, to be located initially in LSHTM, but moved to the 'top floor' of the Cambridge Zoology Department in 1945. It initially included Jimmy (later Sir James) Beament, Tony Lees and John Kennedy (all later to become F.R.S.s) and augmented in 1955 by John Treherne's unit for Neurosecretion. Today's readers may be amazed at the assembly of acknowledged leaders in their various related fields into a common unit. VBW was exhilarated by the new position which stimulated his intellectual development, changed his research emphasis to agriculture, and enabled his return to Cambridge. He became a Professorial Fellow of his old College in 1945. The nucleus of talent on the 'top floor' attracted sabbaticants and other distinguished visitors from around the globe. I recall Carroll Williams from Harvard, who was endeavouring to purify the juvenile hormone from silkworms and had created his famous 'Golden Oil'. VBW drew some lines with the oil on the back of a fifth instar *Rhodnius* which, when fed, developed into a normal adult but with the letters 'VBW' clearly visible in new *larval* integument on its dorsal side. This demonstration encapsulated his talent for simple demonstration of powerful principles. Later, Carroll privately confided to me his view that "VBW had the annoying habit of always being right for all the wrong reasons". I suspect that this gentle rivalry outlasted both men.

VBW was honoured by the Queen with a C.B.E. in 1951. In 1952, he was elected by the University as 'Quick Professor' (named after Frederick James Quick, 1836–1902). The latter inspired the silly poem by John Updike in the New Yorker (V.B. Nimble, V.B. Quick…), which VBW hotly despised. He continued to work in his accustomed independent isolation, but enjoyed the social aspects afforded by his academic stature. He would talk with enthusiasm about his work at the weekly tea meetings on the 'top floor', but only after he had submitted the work for publication. The Quick Professorship required him to take graduate students, a responsibility for which he was both unprepared and reluctant. He received entreaties from around the world. But over time, he softened and opened up to many of his over 50 graduate students and became proud both of them and their achievements. Many later excelled in their own fields, but he was modest in his contribution to their success. "It is hard to know what, if anything, they owed to my supervision", he observed. Students were offered a project and expected to get on with it, following their introductory meeting with him, which sometimes ended with "Don't forget to hand in your thesis before you leave". I suspect that he developed this approach both to require independence from his students and to permit him his accustomed freedom to work in isolation. This approach transmitted to his students the importance of reliance on their own qualities and abilities, as he had done himself. He remained enthusiastic to discuss results and to offer guidance to the receptive. Thereby, students were free to blossom in their own, unique, ways. He would never inflict his views on his students, nor influence their thinking by advocating reading the ideas of others until after they had obtained practical experience of their own. This dependence of intellectual blossoming on imagination and creativity was at the heart of scientific life in the unit. Those few students who felt entitled to instruction were nimbly evaded and confronted with his closed door. But these too prospered, for salvation lay in the ready technical help and constructive criticism that was readily available from the international pool of visitors and staff of the unit, and sympathy in the local pub, The Bunshop. VBW received a knighthood from the Queen in 1964 and he retired in 1967 when the ARC unit was disbanded. As Professor Emeritus in Cambridge, he published an astonishing further 63 papers after retirement, the last in 1992.

Some readers will know me as an author of papers on growth and development of *Rhodnius*. It is relevant here to summarise how this came about, as it intersects with my years in Cambridge, VBW himself and his students. In my first three years in Cambridge, much time was spent in the Zoology Department and I came to know many of its staff and students. *Rhodnius* was a discussion topic at every turn. I became enthralled with its multitude of experimental attributes. I wished to complete a PhD on some aspect of his bug, but unrelated circumstances required that I leave England. My mentors in Zoology proposed one of VBW's earlier students as a potential supervisor, who had recently moved to Queen's University in Canada. He accepted me instantly. I proposed work on *Rhodnius*, which he had eschewed in favour of butterflies, but followed VBW's example of not influencing my decision. On reading the literature I found to my horror, that no work had been done on the brain of *Rhodnius* since VBW's initial findings of 1940, requiring me to study the many neurosecretory cells in the brain by various techniques. The next summer I returned to Cambridge. John Treherne was asking me about my work with *Rhodnius* in the corridor, when a gentle man in a white lab coat appeared behind me, asking "Are you working on *Rhodnius*?" VBW ushered me into his sanctum and engaged me in discussions for over an hour. I returned every summer and always found that long, spontaneous discussions developed with VBW, which became far ranging. After Canada, I returned to England to work on the role of neurosecretion in photoperiodism with Tony Lees, with *Rhodnius* work as a side-line. This position enabled more frequent visits to VBW and his mountains of stories, for a further four years. I realised I had acquired some unclear but special status in his mind, that allowed him to talk freely with me, not just about his career but also his personal struggles and fears. I learned of a very different person from the one originally described to me. I felt both moved and honoured by his confidence. It is now 50 years since our initial encounter, my C.V. contains 50 papers with '*Rhodnius prolixus*' in the title and I hope his spirit is with us to hear that my laboratory is at last hot on the trail of the gene that codes his 'brain hormone'.

Times have changed greatly since those of VBW. But that does not mean science of such great significance cannot be repeated, for the human mind and intellect have not changed. We all solve simple daily problems using hypotheses that are in principle verifiable (i.e. scientific logic), a notion that prompted Huxley (1863) to observe "we are all scientists". The legacy of VBW for modern times lies primarily in the careful thought articulated in all his work. The Introductions to all of his many publications (listed by field of physiology in Locke (1992)), demonstrate that critical analysis of the significance of each problem was the basis for the design of his experiments. With the field of insect physiology an essentially blank canvas, some might imagine that VBW had it easy, since virtually every finding would be novel and publishable. But he eschewed the easy and obvious in favour of areas of insect research that would yield fundamental insights into the physiology of animals in general. It is equally true today that the researchers whose names will live after them are those who invest careful thought into identifying the critical gaps in knowledge of their fields and then carefully designing experimental ways to fill those gaps. It should remain foremost in all our minds that the formulation and evaluation of these crucial ideas must precede implementation of plans to hatch them. The life and work of VBW continue to stand as monumental and enduring examples to us all.

A complete bibliography of Wigglesworth's publications can be found in Gupta (1990) and Locke (1992). The photograph of VBW is from Coaker (1994) © 1994 Association of Applied Biologists, with permission of John Wiley and Sons. Thanks to Dr. Xanthe Vafopoulou for constructing the frontispiece.

References

Beament, J.W.L., 1994. In: Obituary: Professor Sir Vincent Wigglesworth. The Independent, 16 February, pp. 3.

Buxton, P.A., 1930. The biology of a blood-sucking bug, *Rhodnius prolixus*. Trans. Entomol. Soc. Lond. 78, 227–236.

Coaker, T.H., 1994. An appreciation. Sir Vincent Wigglesworth CBE, FRS. 17 April 1899–12 February 1994. Ann. Appl. Biol. 124, 575–578.

Favaro, G., 1925. Contributi allo studio morfologico dell'lipofisi caudale (rigonfiamento caudale della midolla spinale) dei teleostei: memoria con 40 fig. nel testo. Soc. anon. tipogr. "Leonardo da Vinci".

Gupta, B.L., 1990. "VBW90": a birthday present for the journal. Professor Sir Vincent Wigglesworth C.B.E., M.D., F.R.S. 90 years and still smiling. J. Insect Physiol. 36, 293–305.

Hanström, B., 1938. Zwei Probleme betreffs der hormonalen Localalization im Insektenkopf. Acta Univ. Lund, N.F. Avd. 2 (39), 1–17.

Huxley, T.H., 1863. We are all scientists. In: Huxley, T.H. (Ed.), Darwiniana. Appleton Century Company, Inc., pp. 1–16.

Kopeć, S., 1922. Studies on the necessity of the brain for the inception of insect metamorphosis. Biol. Bull. 42, 323–342.

Locke, M., 1992. Professor Sir Vincent B. Wigglesworth. Biography and contributions to insect morphology and embryology for the 1992 distinguished international award. J. Insect Morphol. Embryol. 21 (2), 101–115.

Locke, M., 1996. Sir Vincent Brian Wigglesworth, C.B.E., 17 April 1899–12 February 1994. Biogr. Mem. Fellows R. Soc. 42, 539–553.

Nabert, A., 1913. Die *Corpora Allata* der Insekten. Z. Wiss. Zool. 104, 181–358.

Pflugfelder, O., 1936. Vergleichend-anatomische, experimentelle und embryologische Untersuchungen uber das Nervensystem und die Sinnesorgane der Rhynchoten. Zoologica 93, 1–102.

Speidel, C.C., 1919. Gland-cells of internal secretion in the spinal cord of the skates. Carnegie Inst. Wash. Publ. No. 13, pp. 1–31.

Wigglesworth, V.B., 1933. The physiology of the cuticle and of ecdysis in *Rhodnius prolixus* (Triatomidae, Hemiptera); with special reference to the function of the

oenocytes and of the dermal glands. Q. J. Microsc. Sci. 76, 269–318.
Wigglesworth, V.B., 1934a. Insect Physiology. Methuen, London, pp. 134.
Wigglesworth, V.B., 1934b. The physiology of ecdysis in *Rhodnius prolixus* (Hemiptera). II. Factors controlling moulting and 'metamorphosis'. Q. J. Microsc. Sci. 77, 191–223.
Wigglesworth, V.B., 1936. The function of the corpus allatum in growth and reproduction of *Rhodnius prolixus* (Hemiptera). Q. J. Microsc. Sci. 79, 91–121.
Wigglesworth, V.B., 1939–1972. The Principles of Insect Physiology. 7 English language Editions increasing from 437pp. to 827pp.
Wigglesworth, V.B., 1940. The determination of characters at metamorphosis in *Rhodnius prolixus* (Hemiptera). J. Exp. Biol. 17, 201–223.
Wigglesworth, V.B., 1948. The functions of the corpus allatum in *Rhodnius prolixus* (Hemiptera). J. Exp. Biol. 25, 1–15.
Wigglesworth, V.B., 1952. The thoracic gland in *Rhodnius prolixus* (Hemiptera) and its role in moulting. J. Exp. Biol. 29, 561–570.
Wigglesworth, V.B., 1985. Historical perspectives. In: In: Kerkut, G.A., Gilbert, L.I. (Eds.), Comprehensive Insect Physiology, Biochemistry and Pharmacology, vol. 7. Pergamon Press, Oxford, pp. 1–24.

Colin G.H. Steel,
York University, Toronto, Canada
E-mail address: csteel@yorku.ca.