



Valerie Ann Alabaster 1941-2021

Valerie Alabaster, Honorary Fellow of this Society since 2000, died at home earlier this year, a few months short of her 80th birthday. She had a long and distinguished career in drug discovery in the pharmaceutical industry and made a very significant contribution to British Pharmacology via the BPS, through her work on the education and training of young pharmacologists.

Val, as she introduced herself to all, first encountered Pharmacology in her BPharm course at Chelsea College (now subsumed into King's College London) and was strongly influenced by the enthusiastic and inspirational teaching of Jack Botting, to take up the subject instead of qualifying as a pharmacist. Her response to his encouragement was to graduate with a First Class degree and to start work in the pharmaceutical industry. Val's first job was with one of the leading pharmacologists in industry, David Jack, at Allen and Hanburys (later subsumed into Glaxo) who was searching for a β -adrenoceptor agonist with selective action on bronchial smooth muscle and little cardiac effect, to replace isoprenaline as a bronchodilator in asthma. Val was the first author (under her maiden name) on the paper in the *BJP* (Cullum et al., 1969), that described salbutamol, the successful outcome of this search, and the first selective and clinically effective β_2 -adrenoceptor agonist. This discovery was pharmacologically important on at least two levels. For academic pharmacologists, it showed that the division of β -adrenoceptors into β_1 in cardiac muscle and β_2 in bronchial smooth muscle as proposed by Lands et al (1967) was not only correct but that this division could be turned to practical use to produce a clinically useful medicine. And for asthmatics, it was literally a lifesaver, preventing the often lethal side-effects of inhaled isoprenaline, while providing immediate bronchodilatation. For many asthmatics (and such patients have actually increased in the past few decades), salbutamol (Ventolin in the UK) is still, more than 50 years after its discovery, their most frequent and effective treatment.

In 1967, Val moved to ICI Pharmaceuticals (now part of Astra-Zeneca) in Macclesfield, to work with another major player in catecholamine research, Mike Barrett, before returning to London and academic pharmacology, as a PhD student, with the support of ICI and the Wellcome Trust, a clear recognition of what she had already achieved, and of her potential as a research pharmacologist. For her PhD, Val (now Val Alabaster) joined the Department of Pharmacology at the Royal College of Surgeons, a small research department with no formal undergraduate responsibilities and already punching well above its size in research output. During Val's PhD, the Department was at its most productive period, with Gustav Born leading a MRC Thrombosis Unit exploring platelet pharmacology and John Vane's group analyzing the synthesis and clearance of endogenous vasoactive agents. The work of both groups led to major advances in clinical medicine – low-dose aspirin to protect against intravascular aggregation of platelets and the ACE inhibitors as anti-hypertensive agents - and, for John Vane, to a share in the Nobel Prize. It was a vibrant and exciting atmosphere for any student, and Val with her prior experience in practical pharmacology, was particularly able to contribute to, and benefit from, the variety of ideas, techniques, tissues and mediators that were discussed in the tea-room. Although much of her PhD project in Vane's group dealt with the pulmonary clearance of 5-HT, she also worked with two vasoactive peptides, angiotensin and bradykinin, and was involved in the early characterization of the bradykinin potentiating peptides as ACE inhibitors (Ferreira et al., 1970; *Nature*, **255**; 379-380).

Immediately after finishing her PhD in 1971, Val took up a position as a Staff Scientist at the new research facility Pfizer had just opened in Sandwich, Kent, and remained there until her retirement in 2002, as Director. Over this time, Val was involved in a wide range of drug targets, including α_1 - and α_2 -adrenoceptors, muscarinic M_3 receptors, PAF antagonists and K^+ channel openers. The α_2 -adrenoceptors provided a fascinating and novel area of investigation as they were the first presynaptic auto-receptors to be described and had been postulated to explain the effects of clonidine. This compound also exemplified a then rarely used pathway to drug discovery, being repurposed during development, from a nasal decongestant to an anti-hypertensive agent. Although the α_2 -adrenoceptor project did not yield a drug candidate, Val's team was more successful with the α_1 -adrenoceptors, identifying doxazosin, a selective α_1 -adrenoceptor antagonist, used clinically as an anti-hypertensive agent (Cardura). She then moved to the cholinergic system and was very much involved in the discovery of darifenacin, a selective M_3 receptor antagonist for the treatment of urinary incontinence. A project on PAF antagonists was, like all PAF pharmacology, scientifically rewarding but clinically frustrating. This endogenous lipid has proved to be one of Pharmacology's 'Great Mysteries', exhibiting potent effects on platelets and smooth muscle and generating a great deal of excellent science but, in more than 40 years of study, no clinical applications.

Val's responsibilities expanded over time to lead more projects, as Director she became responsible for about 70 biologists, spread over different target areas (respiratory, gastro-

intestinal and urogenital) but she maintained good contact with her teams and was respected at all levels, particularly for her freely given, fact-driven, thoughtful and helpful advice which was much valued by project scientists. The drug the public most associate with Pfizer is sildenafil (Viagra; UK92480) and Val's contribution to that discovery was indirect but important, providing another example of repurposing, at an early clinical stage, just like clonidine. Sometime before UK92480, designed logically as a PDE5 inhibitor, was tested clinically as an anti-angina treatment, Val had led a team to assess impotence as a worthwhile drug target. The results of the typically thorough and detailed assessment identified impotence as a real but understated clinical problem. However, there was, at that time, no way of converting the known physiology and pharmacology of penile erection into a clinically viable treatment. So, once her analysis was completed, Val returned to her ongoing projects. When the first clinical results with UK92480 showed it was unlikely to make the grade as a coronary vasodilator, but a frequent and totally unexpected side-effect was penile erection, with onset soon after taking the drug, the significance of these side-effects was quickly appreciated and another example of successful repurposing was added to the drug discovery literature. According to Pasteur, 'Chance favours the prepared mind'; here the UK92480 team recognised the chance observation and Val's team had helped to prepare the mind.

Val was a role model and mentor for many of her younger colleagues and was particularly known for her support of women at Pfizer, at a time when such support was much less common than nowadays. This led to her involvement with the Daphne Jackson Trust which enables scientists, most often women, to return to research after career breaks. As an Industrial Advisor to the Trust, she provided valuable insights into STEM careers in a commercial organisation, to inform and guide the Trust. In more practical terms, Val was able to secure places for five Daphne Jackson Fellows to be hosted and sponsored by Pfizer, at the Sandwich site, over a period of 10 years.

Throughout her career in drug discovery, Val was also an active member of the BPS, attending meetings, presenting results and training her younger colleagues in the arcane mysteries of Oral Communications which were, in the early years, a prerequisite for membership of the Society. Her commitment to Pharmacology was also expressed by her strong support for industrial placements for undergraduate and postgraduate students (via MRC/BBSRC and CASE awards). For undergraduates, Val particularly recognised the value of placements to increase their lab skills, along with their general knowledge of drug discovery in industry. On graduation, many such students were offered their first position in the lab where they had spent their placement year.

Val was a member of the BPS Committee (1985-1988) but her most important contribution to the Society was through its Education Committee. During the 1990s and into the new millennium, she led that Committee and the BPS *In Vivo* Training Group, bringing together senior scientists from academia, pharmaceutical and biotechnology companies, to ensure that Pharmacology teaching and training could provide the knowledge and skills necessary to drive forward not only the science but also drug discovery. One outcome was an article (*TRENDS in Pharmacological Sciences*, **23**, 13-18, 2002), emphasizing the continuing value of

in vivo pharmacology, as knowledge of molecular biology and its application to drug discovery increased. Another, more practical and crucial outcome, was financial support from industry for teaching *in vivo* skills in university courses.

Although her colleagues recognized her total dedication to drug discovery, and to education, training and career development in Pharmacology, they also knew Val's professional excellence was combined with an active sense of humour and of fun. The inevitable committee and project meetings ended with decisions, but they also involved a lot of laughter. Her colleagues found working with Val downright enjoyable, regardless of the success of the programme. She made many friends and kept them; the Alpha Girls started as a social group in the early days at Pfizer and they were still getting together until the second wave of COVID-19 put an end to such frivolity. Her answer to questions about her plans for her retirement was typical, "I think I shall grow old *dis-gracefully*".

It was also typical of Val to be as busy in retirement as she had been at Pfizer, although her time was taken up with a different set of concerns. She continued advising the Daphne Jackson Trust for another 5 years after leaving Pfizer, while completing a course in counselling which she put to use with the local branch of Cruse, a charity providing bereavement care. Val also contributed her organisational abilities to Cruse, as Chairperson she supervised the merger of her branch with another, while minimizing any loss of service. During this time, she also acquired a competent fluency in Portuguese because she and her husband had an apartment in the Algarve, in easy reach, not of the beach, but of a golf course (for Colin) and of walking country (for Val). Walking was a serious occupation for her, both in Portugal and in the UK, where she was a group leader for the local Ramblers. Her electric bike was however essential for another fun part of retirement, for trips to the pub, to meet other ex-Pfizer colleagues. The pandemic, as it did for many, took a lot of the fun out of life, but the calls for counselling were unabated and she was still an active member of Cruse up to a few months before her death.

She is survived by Colin, her husband for 53 years, two children, Jo and Matt, and four grandchildren.

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I am deeply indebted to Val's family and to her many colleagues and friends who have provided, at a difficult time, much of the background for this Obituary.