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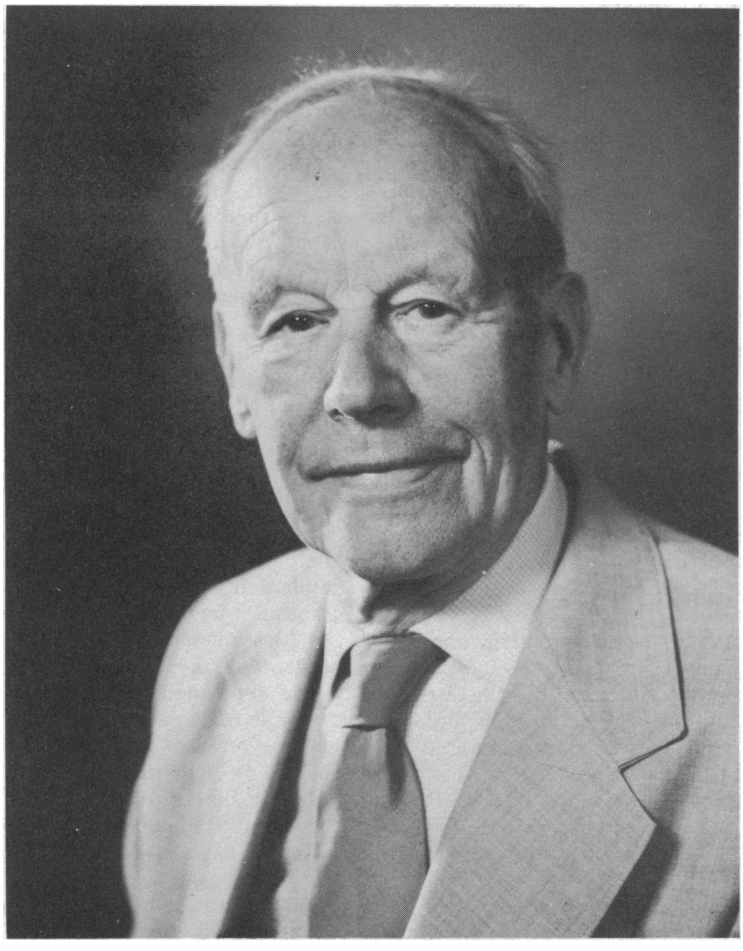
# J.H. Burn: an appreciation



Joshua Harold Burn, Emeritus Professor of Pharmacology at Oxford, died in his ninetieth year on July 13th, 1981.

Those who worked with Harold Burn will always have their own vivid and very personal memories of him but there are hundreds of others who knew him personally, and thousands who did not, who will never forget this exceptional man. And there are perhaps tens of thousands, including those in future generations who will be influenced by what he was, by what he wrote and what he did. If anyone can be said to have moulded the subject of pharmacology around the world, it is he. He did this through his particular style of research, through the lucidity of his writings but most of all through the school which he founded. Young, impressionable scientists from various disciplines and older, not so impressionable, pharmacologists all came to work with him. They found inspiration in working with him, caught his enthusiasm for pharmacology and then returned to continue their research elsewhere in the world in universities, institutes, in clinical medicine and in industry.

Based on a memorial address given in the chapel of Balliol College, Oxford on October 17th, 1981.

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In this personal reminiscence, I shall concentrate on the period when he was at the pinnacle of his career in Oxford and only briefly refer to his early life. Well before the first World War, he trained in Cambridge, and was influenced by J. Barcroft, F.G. Hopkins and H.K. Anderson. He then went to work with Henry Dale at the Wellcome Physiological Research Laboratories in January 1914, but after a few months joined the army for war service. He completed his medical degree in 1920 and immediately rejoined Dale, who by then had moved to the National Institute for Medical Research. He learned many things from Dale, including the ability to letter in copperplate with a white ink on varnished kymograph paper. This period was very important to his career. From Dale, he acquired the experimental skill for which he was renowned and the ability to write scientific papers which were always clear and stimulating. But there is one other practice which he also learned from Dale and that was – and I quote Harold Burn – 'that daily lunch together is an essential part of laboratory life if workers are to profit by what they can learn from each other'.

He was with Dale for 5 years working mainly on biological standardization. This formed a basis for his appointment as the first Director of the Pharmacological Laboratories of the Pharmaceutical Society, a position which he took up in January 1925 and held for twelve years. In this, his first department, Burn pioneered the use of statistical methods in pharmacology, especially for the bioassay of hormones and vitamins. He recognized that the imprecision associated with biological variation – the essence of life which makes one animal or person respond differently from another – could be largely overcome by applying statistical analysis, more precisely to define the limits of the variation. In 1937, he published a book on biological standardization (Burn, 1937) which became the accepted text in the field. It was later translated into German and much used in Russia.

During this period, he was also engaged on physiological problems which interested him much more than standardization. One involved tyramine and another involved sympathetic cholinergic fibres, subjects to which he returned later.

Having built a strong and widely acclaimed department at The Pharmaceutical Society, he moved to Oxford in 1937 and was Professor of Pharmacology there for more than twenty years. He gathered around him a team of the most talented individuals. From London he took with him Harold Ling and Edith Bülbring and then in the 1940's attracted many others, including John Walker, Hugh Blaschko, Miles Vaughan Williams and Harold Ing; all those named stayed with Burn until he retired and with Oxford until they did.

His laboratory gradually became the most active and important centre for pharmacological research in the U.K. and the main school for the training of young pharmacologists. He was recognized as being remarkably successful in discovering promising young beginners and giving them an opportunity to start work. I well remember, a few years ago, when I was discussing with him the many people he had trained and who had become successful pharmacologists, he chuckled and said that perhaps he *did* have a talent for spotting the promising young scientist. He was, I think, displaying a similar modesty to that of Michaelangelo, who, when congratulated on having produced a beautiful sculpture out of a block of stone, shrugged off all compliments. 'It was there all the time', he said. 'It just needed someone to come along and uncover it.' Burn was likewise modest about his students, but they only really became promising young scientists as he chipped away at them with his chisel.

He was the scientific father of an enormous family. I cannot over-emphasize the influence this great man had upon the developing science of pharmacology through those whom he taught and shaped. Incredibly, the list contains more than 160 names. Even more incredibly, more than 60 of these, in many different countries, became Professors or Directors leading internationally recognized research groups in their own right. Those 160 people each became implanted with the gene of Burn's enthusiasm and inspiration and they in turn have passed it on or are still passing it on to a whole new generation of students. Many of Burn's scientific children became world renowned. His scientific grandchildren will continue to carry the gene and to pass on part of the essence of Burn's attitude towards science and research. It is in this way, as well as in his actual research, that Burn's influence will continue to be felt throughout the generations of pharmacologists who never met him. Amongst those who had the good fortune to work with him, there is a strong sibling bond and a great affection for the father figure.

I came to his department in 1946 with a chemistry degree, with no biological training of any sort and with little or no motivation to stay in science. A month to the day after joining, I was summoned to his office, given a dressing down and told 'You'll have to go if you don't improve'. Despite the generality of the admonition, I must have improved in the way he wanted for I stayed, and was turned into a fairly professional pharmacologist. That particular event had a significant influence on me, as indeed, it must have done on many others, for in talking to my colleagues (as we did in the department into the late hours of the night after a two shilling meal at a British Restaurant) I soon discovered that every single one of them had received the same message that 'they

would have to go if they didn't improve' four weeks after their arrival!

Looking down the list of people who worked with Burn I can count more than twenty whom I met during that two year period whom I still value as friends today and a much greater number whom I met between 1949 and 1953 when I was doing my D.Phil. with Geoffrey Dawes at the Nuffield Institute and visiting the Department as a demonstrator.

I mentioned earlier that daily lunch together was regarded by Burn as an essential part of laboratory life. It soon became clear to all of us who came naive to this custom that it was, indeed, a most useful adjunct to the learning process. The L-shaped table in the library with Burn presiding at the top and us junior students at the bottom, was an integral part of the development of a visiting worker or a student. Lunch time conversations ranged over many topics, often becoming informal debates amongst the senior staff from which we youngsters profited simply by listening. And on occasion, we were all enchanted by recitations by Harold Burn, who seemed to hold in his memory all of Gilbert and Sullivan and of Gilbert's Bab ballads. In his book, 'The Background of Therapeutics' (Burn, 1948), he points out that the disappointing effect of exercise in treating obesity had been discussed by W.S. Gilbert–

'Most people think that, should it come,
They can reduce a bulging tum
To measures fair
By taking air
And exercise in plenty.'

Everyone who passed through the laboratory either as a casual half hour visitor, or as a research worker or student, could not fail to be impressed by the weight of Burn's authority. His students held him in great respect if not in fear. As well as being a king-maker, he was also king in his own castle. And when the authority was tinged with temper, the laboratory family sometimes felt the strain. I well remember the day when we all, from the highest to the lowest, found ourselves sweeping the floors and cleaning the benches of the Department because, in showing an important visitor around, Burn had found a particular piece of apparatus was not as clean as it should have been. I am not sure whether I ever admitted that I had been the last to use that piece of apparatus!

His method of teaching new students was both elegant and simple. Each would be charged to discover the full pharmacological properties of a drug or chemical which interested him. In this way, the newcomer would learn to use all of the pharmacological methods available in the laboratory. In the process of so doing, an unexpected observation might lead to a new train of thought and to a new series of experiments.

Although I have dwelt on Burn's contributions through the active school which he founded, this in no way belittles his other contributions to pharmacology. He was a foundation member of the British Pharmacological Society from 1931 and played a leading role in its affairs until he retired in 1959. He became Secretary and Treasurer of the Society in 1934, became an editor of the newly founded British Journal of Pharmacology in 1945 and acted as Foreign Secretary for the Pharmacological Society for twelve years from 1947. He was a Trustee of the Society from 1965 until he died. He was also active in the Physiological Society of which he was twice a committee member and was the British representative on the International Committee of Pharmacologists, the forerunner of the present day International Union.

Thus, Burn contributed greatly and uniquely to the development of the science of pharmacology through his teachings and through his activities within the British Pharmacological Society, a society which incidentally he entertained in Oxford six times during his reign as Professor.

Burn was also a man with a strong social conscience. Long before it became fashionable, he was actively campaigning against smoking, especially in the laboratory. With one scientist, he had little success. On one occasion, he said 'Bill, you can't work at the bench and smoke at the same time', to which Bill answered 'I agree, Professor, and if you look carefully, you will see that I'm not working.' On another, Burn said, 'Bill, every time I see you, you are smoking a cigarette'. Bill answered, 'That's because you make me nervous, and every time I see you coming, I have to light one!'

Burn believed that people should be paid according to their needs. If there were two people equally qualified in science and one was married, he believed the married one should be paid more. This attitude led to an unfortunate introduction into the laboratory for a Canadian who came to study for a D.Phil. Unbeknownst to Burn, his last act before leaving Canada was to get married and the bride and groom enjoyed their honeymoon on the ship coming over. They both came straight to the department, only to be reprimanded by Burn for the irresponsibility of getting married. His wife was told that she shouldn't be here, for they couldn't afford to live in Oxford on the grant that Burn had arranged for him, expecting him to be single!

I have left until last Burn's contributions as an original researcher. There was one field to which he always returned and for which he will surely be remembered best, the investigation of autonomic neurones, much of it performed in collaboration with

Edith Bülbring. There was always an air of expectancy and bustle created in the lab whenever the Prof. was going to do an experiment. He had an eye for the unusual observation, one that could not be fitted easily into current theory. He also had a long memory for earlier observations, developing them at a much later time. Thus, his third scientific paper in 1915 was on the action of an alkaloid called conessine. He gave the same substance thirty years later to a bright young newcomer to develop further the pharmacology that was then known. Again, in the early thirties, he showed (Burn & Tainter, 1931) that tyramine had less activity than expected when tissues were deprived of their sympathetic nerves. Over the years, he returned many times to this observation until in 1958, in a classical paper, written jointly with Mike Rand (Burn & Rand, 1958), he first made the general distinction between those sympathomimetic amines which acted directly, such as adrenaline and noradrenaline and those which acted indirectly through the release of pre-formed adrenaline or noradrenaline from stores.

He was not afraid of controversy, nor of delivering strong and sometimes impetuous opinions. Many a meeting of the Physiological or the Pharmacological Society was enlivened by his questions, judgements or accolades of his peers. One of his most striking characteristics was his ability, by the publication of unorthodox ideas and hypotheses, to stimulate others to initiate experiments which they otherwise would not do, His work on the cholinergic nervous system gradually brought him to the view that acetylcholine served not only as a chemical transmitter of nerve impulses in the parasympathetic nervous system but also as a local hormone involved in transmission of other rhythmic movements. Thus, he linked acetylcholine as a local hormone to the movement of cilia and to the beating of the heart. No matter whether his hypotheses were right or wrong, they created a climate which others could not fail to challenge. Thus, some pharmacologists were stimulated to spend a substantial part of their research career trying to prove or disprove the views of Burn. Perhaps the most interesting example of this, and certainly his most controversial idea, came with his proposal, along with Rand, that acetylcholine was a co-transmitter with noradrenaline in sympathetic nerve fibres. This hypothesis (see Burn, 1971) became notorious around the world as the 'Burn-Rand hypothesis'. After his retirement from active research in Oxford, he continued to persuade others by visits and by letters, to do experiments to prove the hypothesis. He became a passionate champion of the hypothesis and even after his eightieth birthday party in 1972, in Worcester College (an event which he described as 'literally the occasion of his life') he wrote to say that he now had letters from Loewi, Bard, von Euler, Granit and Heymans, all supporting the Burn-Rand hypothesis. Nevertheless, it did not become generally accepted.

Would that he could have attended the 50th Anniversary Meeting of the British Pharmacological Society, in Oxford, in September 1981. Had he been there, he would have been delighted that a whole morning's symposium was devoted to the concept of co-transmitters in nerve fibres and he would have been justly proud to hear the Burn-Rand hypothesis often quoted. Clearly, he was a man who not only dominated the pharmacological thinking of his time but also, in the last analysis, made important contributions which were ill-received because they were ahead of the thinking of his time.

Professor Burn received many honours and accolades in recognition of his achievements. These included the Fellowship of The Royal Society, numerous memorial lectureships, four prestigious honorary degrees, the honorary presidency of the International Union of Pharmacologists, and honorary membership of the British and other Pharmacological Societies. He was particularly pleased to be awarded by the British Pharmacological Society in 1979 the first Wellcome Gold Medal in Pharmacology. He wrote ten or more books dealing with pharmacology and its applications and was the author of several hundred research papers and reviews.

In 1969, Harold Burn wrote an article entitled 'Essential pharmacology' (Burn, 1969). That title in itself is a fitting epitaph for the man. To quote from that article, he says: 'Finally, would I choose a different career if I had my time again? After all, it can be said that those who spend their lives in research leave little behind them. They are not sculptors or painters whose work may be preserved for hundreds of years. On the contrary, their research, whether of their earlier years, or even of ten years ago, is forgotten while they are still alive. Nevertheless they have their consolations. I can think of no way of spending life with more satisfaction that it was spent in the Oxford department, where we met for a brief break at 11 a.m., later for lunch in the library, and for tea at 4.15. At one period there was a grand piano, and there were two who played Mozart, Beethoven and Haydn as duets. We were a community like a College Common Room, and at the same time all (or nearly all), very interested in our research. There was usually a good sprinkling of workers from abroad so that we felt ourselves an international group. Moreover, our work was mostly of the kind that required hand skill, and gave an opportunity for some artistry in execution. I have a letter from a one-time statesman (Lionel Curtis) saying that the Vice-Chancellor (at that time Richard Livingstone) had told him we were the happiest family in Oxford. We used to have the Vice-Chancellors to lunch; they were all Arts men,

and we wanted them to see what the scientific life was like. Thus I am quite certain that I would choose to have it all over again.'

Clearly, I and many others would disagree with the idea that those who spend their lives in research leave little behind them. Some, including Professor Burn, sculpt with great mastery, but using flesh and blood as material. Harold Burn could *not* be forgotten whilst he was alive. And now, because Harold Burn combined the talents of producing innovative research, of teaching, of inspiring, of enthusing, of stimulating others, he will *never* be forgotten. He was not only 'essential pharmacology' he was essential *to* pharmacology.

*J.R. Vane*

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