

This is a tribute to John R. Fozard, PhD, who passed away after a long and courageous fight with disease, on September 29, 2018 in Hegenheim, Alsace, close to Basel.

### **Bradford and Manchester:**

Christine Fozard: We have received so many tributes to John from colleagues, collaborators, ex-students: all spoke of his professionalism, his influence, his enthusiasm, his passion for his science and his influence on pharmacology in general, because he was always a general pharmacologist and one of the last few to do so with a degree in Pharmacy, not Medicine.

Few people have known him throughout his whole career – so here goes with one or two “secrets”! John’s first degree was from Bradford CAT. This was an external London degree – which made his Mum so proud as it was presented in the Royal Albert Hall by the Queen Mum! She was not so impressed when he was presented with his PhD by Harold Wilson in Bradford Town Hall.

John did his first degree at Bradford and then wished to move to America, but his supervisor refused to let him go. So, he took the huff and moved to Manchester, which is where we met, I a new undergraduate in Pharmacy (the first, you might say, of his students), he a very low junior lecturer (enough said).

While at Manchester he worked with a grant from the migraine trust, with little success, but a good social life. We married in 1969, after I passed my final Pharmacy exams, (second time around). We also had a sabbatical year in Mainz in 1970-71 (another language to learn).

Thus, John Fozard graduated in Pharmacy from Bradford where he started his PhD, moved to Manchester (1967) as an assistant lecturer with his PhD still in the works. To quote David Clarke: “Good men are few! I taught John as an undergraduate at Bradford and put him on to his PhD on 5-HT — he never looked back. I worked the other side of the bench from John and spent many hours discussing and arguing over science. The discussions were made easier as his father was a butcher and we had daily warm pork pies the chew on”. After completing his PhD in Manchester (submitted to Bradford), and getting married, he won a Fellowship from the DAAD (Deutscher Akademischer Austauschdienst). It was with leave of absence from Manchester that he went to spend a year with Prof. Erich Muscholl, the well-known and at times, feared Head of the Institute of Pharmacology in Mainz. Upon his return, John spent several years in Manchester.

Gareth Sanger recalls: “John was a lecturer at Manchester in Pharmacology when I was a PhD student upstairs in Physiology ... At the time, we never understood why anyone should ever be interested in the actions of 5-HT within the sympathetic nervous system... After my first presentation to the British Pharmacological Society, I remember both John and Barry Cox treating me with fatherly kindness, gently correcting a glaring error in my presentation. Later when we were both working in different drug companies, the same kindness showed itself, sending me compounds, including MDL72222 (unheard of today, without a team of lawyers getting involved) and again, making me feel like I was talking to a mentor as I stumbled over the language of pharmacology.”

Arthur Weston: I knew ‘Fozzy’ very well indeed, especially during his many years in Manchester, starting in the late 1960s. There was nothing he did not know about 5-HT; he was at the forefront of this-then rapidly-developing field. As his career progressed at Merrell and then Sandoz/Novartis, he became (and remained) a world-authority on all things tryptaminergic. Especially during his academic career, he supervised many PhD students with critical and painstaking attention to their experimental design and when in ‘BigPharma’, he was responsible (probably over a period of two decades and perhaps more) for making many 12-month industrial placements available to UK honours pharmacology undergraduates. There will be dozens of now-mature pharmacologists who owe their subsequent successes and careers to Fozzy’s influences. With his passing,

the British Pharmacological Society has lost a 'big' pharmacologist, whose contribution to so many areas of drug development and current clinical practice cannot be over-estimated. After his long and debilitating illness, may he now rest in peace.

Thus, while in Manchester, John worked his way upwards to attain a position of senior lecturer and was then offered a research post in the then Merrell Richardson Research Centre in Strasbourg. So, John, Christine, Ruth and Lucy upped sticks for Alsace and the rest is pharmacological history. When they moved to Strasbourg in 1977, John and Christine owed so many dinner invitations that they had a concentrated period of two weeks of dinner parties - every other night a different group of people, and each time a different menu!

### **Strasbourg:**

M. Spedding: John was like a father to me. I arrived a very young scientist in his department at Marion Merrell Dow in Strasbourg in 1978 and there then followed the eight years which my wife Ann and I will always consider as the best years of our lives, scientifically, socially, even oenologically and meteorologically. Because our apartment wasn't ready, we stayed with John and Christine, and a very young Ruth and Lucy, for a couple of months: a typical example of their generosity, and a great way of getting to appreciate them.

John's Yorkshire humour and down-to-earth sheer decency were a constant encouragement, while his scientific rigour and organisation were a hurdle which made you jump higher and higher. If I have succeeded in any way in science it is because of this example, pressure and encouragement.

John structured great swathes of pharmacology academically, while still discovering drugs which have had a lasting impact. He did much of the work which defined 5-HT<sub>1A</sub>, 5-HT<sub>3</sub>, 5-HT<sub>4</sub> receptors and the great 5-HT review has been quoted more than 3500 times, the most citations of any receptor review. His research team in Strasbourg was highly effective, yet all the work was great fun, and also backed up with many parties or barbeques at 'les Fozards'. His ability to create great links with his technicians as well as his scientists was remarkable. Furthermore, all the scientists in his group made a major impact. Pharmacology at Merrell Dow was one of THE addresses in the 1980s, thanks to John's leadership. His work at Novartis then followed on but in different directions, where his unique approach ensured that pharmacology was a key factor in drug discovery.

John was immensely scientifically eclectic. He developed the Merrell Dow drug eflornithine using totally original pharmacology, allowing it to be used for sleeping sickness, where it is a WHO essential drug. The drug was so effective that the clinical trials were difficult to analyse, because patients were brought in from the African bush, on stretchers asleep, then just woke up with the drug and went back into the bush, stopping follow-up! He developed the concept of 5-HT<sub>3</sub> antagonists, first for migraine, and later for blocking sickness in cancer chemotherapy patients; now a standard therapy of immense use. We were all involved in this work, and I remember interviewing job candidates with an i.v. line in and 5-HT wheals on my arms to test his (ethically approved!) 5-HT<sub>3</sub> antagonist... The 5-HT<sub>1A</sub> drugs owe much to his pioneering work. I remember giving a presentation on a joint project we had worked out and because of John's science, the work was used for exam questions for decades of students.

### **Basel, Alsace and Horsham**

D. Hoyer: I met John Fozard for the first time on September 25, 1981, the afternoon of my thesis defence in Strasbourg, as Günter Engel and I visited John's Institute. A few weeks later, I moved to University of Pennsylvania for my post doc, and we kept in touch ever since. We exchanged letters (no emails in those days) over serotonin research (totally new to me) and many other subjects of interest. Subsequently, I joined Sandoz in 1983 to work precisely on 5-HT. From then on, we would meet regularly at

conferences, especially of the British Pharmacological Society and John would very kindly introduce me to all known leaders in the 5-HT field and many others.

In 1986, we approached John for a leading position at Sandoz, and we would have a couple discrete lunch meetings at my house. By 1987 John was in Basel, and we started working together, although I subsequently moved to Neuroscience Research. 1987 was also the year of the IUPHAR meeting in Sydney and the first serotonin meeting on Heron Island, that was attended by Brian Richardson, Günter Engel, John and most of the tenors of 5-HT research. John was the Australasian speaker of the Society and toured Australia and New Zealand.

In 1990, John organised the very successful Basel Serotonin meeting, a satellite to IUPHAR 1990, where a lot of like-minded people met. The meeting was so successful that the financial proceeds constituted a solid and long-lasting basis for the sustainability of the Serotonin Club, which became an entity with up to 700 members across the world. The club (now known as International Society for Serotonin Research), is still well and alive 28 years later and meets at least every 2 years internationally. It is also in Basel in 1990, that we formally created the nomenclature committee for 5-HT receptors (to be followed many others).

This nomenclature group continued to work intensely under the leadership of Pat Humphrey: by 1992, we were redefining the classification of 5-HT receptors, in a series of communications that culminated in 1994 with a review co-authored by John and several of us, that is one of the most cited pharmacology papers ever published.

Years later, this had become a major activity for IUPHAR, with regular meetings under the leadership of Paul Vanhoutte, in Paris. These early efforts culminated with the *Concise Guide to Pharmacology*, edited every two years by IUPHAR/BPS, the most complete and most accessed Pharmacology database in the world.

As Brian Richardson recalls, John left Strasbourg and travelled 120 Kms south to join Sandoz where he headed up a very large research group focussed on discovering improved therapies to treat various cardiovascular diseases. John realised immediately that modulating 5-HT receptors was unlikely to be productive for these particular clinical indications, but launched a highly innovative approach through adenosine receptor modulation which led to clinical trials of drugs that not only reduced blood pressure, but also corrected metabolic disturbances such as diabetes and obesity which are common in these patients. In 1993, John took charge of the respiratory disease programme at Sandoz which at that time was very much in its infancy and he developed novel concepts for treating asthma and chronic bronchitis which became the cornerstones for a research programme that he led beyond the merger of Sandoz with Ciba-Geigy to form Novartis in 1997. His new Respiratory Research Centre was based in Horsham, about 60 Kms south of London, where he built a powerful group that became recognised as the world's most innovative drug discovery group in respiratory medicine. During this period John commuted from Hegenheim in Alsace to Horsham on a weekly basis. His failing health forced him to relinquish the post of Institute Director which was then filled by John Westwick. John took up leadership of a smaller group in Basel, where he was given his well-earned scientific freedom to pursue whatever he wanted in the respiratory area. He grasped the opportunity and in a brilliant series of investigative studies, demonstrated that activation of sphingosine 1 phosphate receptors was the cause of airways hyperactivity, a cardinal feature of asthma. This has led to a potentially breakthrough approach to treating severe asthma which still causes thousands of deaths each year, particularly in children. These receptors are now one of the main drug targets in immunopharmacology.

John still made frequent trips to Horsham, where he would act as leader, adviser, mentor, friend to the newly hired scientists and to Management, as he was consistently doing in Basel, and previously in Strasbourg.

John was nominated Novartis Distinguished Scientist, the highest accolade for scientists at Novartis, a testimony to his mentorship to so many students and colleagues, to his endless capacity to embrace new research themes, and to successfully translate his research into drugs that would impact so many patients in so many different fields. John was a fellow and honorary member of the British Pharmacological Society, he was the Society's visiting fellow to Australia, and received many other honours.

The retirement party for John, in Horsham in 2005, was attended by well over 150 eminent guests from all over the world, colleagues and friends for Academia and Industry, from Novartis, but also from other big Pharma and Biotech, former colleagues and many mentees. John was a fantastic scientist, friend and Mentor.

We must also say a word about the way he faced up to his last major challenge, Parkinson's Disease, which he had for more than 25 years. He mastered this for longer than anybody we know or have heard of, using his original and highly intelligent way of ensuring that he did not desensitise his dopamine receptors. Eventually the disease became too much even for him, but we know of nobody who has put up such an intelligent, spirited and determined fight.

All this time he was so proud of his family, Ruth, Lucy and Stephen, also his garden, and the Porsche Boxster, an echo of the little MG Midget sports car he courted Christine in, many years ago. Throughout the years in Basel, John kept a vivid interest in good food and wine and good company; many guests and friends will remember memorable lunches and dinners organised by John and Christine, where science, life, arts and politics would be discussed in much opinionated manners.

Pharmacology all over the world is grieving, as are his friends and family. But we must remember his immense contributions, and particularly his smile. The massive number of messages from scientists all around the world are a testament to his universal impact, with many underlying themes: a great gentleman, his smile, his way of calling a spade a spade, which gave spades their place in the world, but charged with humour. One cannot underline enough his scientific impact, from Manchester Pharmacology, where he made a great mark, to Merrell-Dow in Strasbourg, to Novartis in Basle. A few of the very many quotes that describe our personal and collective loss:

**Mark Tricklebanck:** "I feel like he was my dad",

**Tom Blackburn:** "I learnt so much about drug discovery and development from him. A wonderful man".

**Pat Humphrey:** "John was a long-lasting friend and colleague who lived and breathed Pharmacology. He inspired many and was a creative drug discoverer. He will always be remembered with admiration and affection."

**Brian Richardson:** "John played the "piano" of pharmacology with all fingers of both hands. .... Very many colleagues and students benefited from his wisdom and mentorship during his long and distinguished career, ... his impact on the field of pharmacology generally and drug discovery in particular will fortunately continue to be felt for many years to come."

**John Westwick:** "... he was a very honest guy who would not pull any punches, great pharmacologist, very clever with a strong sense of Yorkshire "canniness", I learned a lot from John."

**Terri Branchek:** "The world has lost a gentleman and a scholar. We have lost a mentor and a friend."

**Carlos Villalon:** "I came across John's ingenious and sophisticated lines of pharmacological reasoning in the late 80's/early 90's during my oral presentations at the British Pharmacological Society's meetings and Serotonin Club meetings. Being an in vivo cardiovascular pharmacologist dealing with the direct and sympatho-inhibitory/excitatory actions of 5-HT, John always had the burning (but kind) questions for me in his typical and perfectly clear English accent. But his genuine interest always

went far beyond the scientific sessions with additional scientific advice and donation of serotonergic agonists/antagonists for me. I will always remember John's supportive mentorship as well as his exemplary and impeccable reports when acting as referee or editor of my submitted papers; his writing style was beautifully unmistakable, i.e. Fozard's style!"

**Richard Green:** "John was such a lovely man, always good to be with and talk to and also a truly remarkable pharmacologist. The comments of all of us receiving this news, emphasises these points. He touched our lives always in positive ways"

**Paul Vanhoutte:** "John was such a gentleman in life and in science"

**Allison Abbott:** "John was a member of my editorial board at TiPS and gave me advice, help and support well beyond the call of duty. He was also a beautiful writer."

**Charles Marsden:** "Very sorry to say good-bye to such a great scientific friend and also such a great companion, an infectious sense of humour and no one better to enjoy a meal with."

**Mike Moskowitz:** Can't help but feel a great sense of loss. I met John in the early 80's and an instant long distance friendship developed. I counted on him, he knew his stuff, was a straight shooter and was very helpful to me. ....a wonderful family man to be missed by so many.

Thanks, John, for everything you were to your colleagues, your friends and your family and as many of you mentioned, we will forever remember your smile.

Danny Hoyer, Brian Richardson & Michael Spedding

