

VIDEO INTERVIEW TRANSCRIPT

## Green, Richard: transcript of a video interview (17-Dec-2015)

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## Green, Richard: transcript of a video interview (17-Dec-2015)\*

**Biography:** Professor Richard Green PhD DSc (b. 1944) completed his PhD (1969) with Gerald Curzon and following two years at the National Institute of Mental Health (NIMH), Washington, DC, with Erminio Costa, he joined David Grahame-Smith at the Medical Research Council (MRC) Clinical Pharmacology Unit in Oxford becoming Assistant Unit Director in 1981. In 1986 he was appointed Director of the new Astra Neuroscience Research Unit in London. In 1996 he was appointed Director, Global Discovery CNS & Pain Control, for Astra. After retiring from AstraZeneca in 2007, he has continued psychopharmacology research in Nottingham, and is currently Honorary Professor of Neuropharmacology at Nottingham University. He was awarded the DSc by London University in 1988 and in 2010 was given the Lifetime Achievement Award by the British Association for Psychopharmacology. He is a President Emeritus of the British Pharmacological Society and a former President of the Serotonin Club.

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### [1]. BECOMING A PHARMACOLOGIST

I became a pharmacologist basically because I had a father who was a biologist, he was an entomologist, and I never thought of doing anything else other than some form of biological science. I also quite enjoyed chemistry, which he didn't, and I therefore wanted to combine biology and chemistry and thought I would like to do biochemistry as a degree and into research.

My degree was in chemistry and physiology, it was a joint honours degree, enjoying particularly the more organic chemistry rather than inorganic, and certainly not physical chemistry. My mathematics is not that good. And then got an offer to go and do a PhD with Gerald Curzon at the Institute of Neurology, and he wanted the study really of corticosteroids and their effect on tryptophan metabolism and the brain and brain serotonin levels, with regard to research in depression. And that absolutely hooked me then on neuropharmacology as the rest of my career, and, I think, unlike some people who expect to move areas, I've been fortunate in doing work in neuropharmacology for my whole career.

### [2]. WHAT IS PHARMACOLOGY?

I'm not sure I would like to say what pharmacology is like. Having been a pharmacologist for getting on 50 years and seeing changes, they've been considerable, I think, but I can still see what I'm doing now in what I was doing in the early days. I'm doing things with new techniques, with new approaches and obviously with much more knowledge, but all the work that's coming on with genetics and with molecular biology, I find make it very difficult to discern what directions it might go in.

I've just come from the latest British Pharmacological Society meeting where we've seen our membership approach 4,000. We have a lot of young people. It suggests to me that pharmacology is going to have a big place in UK science for a long time to come, partly because I think now we are trying to make sure we interact with other societies as much as possible. We're holding more joint meetings with the British Association for Psychopharmacology that I've also been much involved with, with the Physiological Society, with the American Society. So by, well I think going back to John Gaddum's comment that the

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pharmacologist is ‘a jack of all trade and a master of none,’ you know, we’re following his ideas from 40-50 years ago and providing a pharmacological approach to everyone’s science, and that has to be good.

### [3]. THE BRITISH PHARMACOLOGICAL SOCIETY

The British Pharmacological Society has always been a major part of my life. I joined in 1973, when it was very much a career step that after you got your PhD and you’d published a little, you would be expected to join the Society and it was the main, to use again a current technique, networking opportunity you had. It could also be quite frightening because you had to present, orally, there weren’t such things as posters, and people would ask you questions and since the abstracts were going to be published by the Journal, would correct your abstract and make sure that it was correct even down to the last comma sometimes. And I was fortunate, I got involved in helping to organise the 1981 meeting, the 50<sup>th</sup> anniversary meeting, and I think that led on to me being offered the position as Meetings Secretary, and that in turn you were expected to move on to becoming the General Secretary, which is now called ‘President’. I rejoice in the title of ‘President Emeritus’. They made it up to us by only being called a ‘Secretary’. Something I enjoyed enormously because I met huge numbers of people outside my own area of interest, and got to know a large number of pharmacologists in the country. And, recently, I went back as a Member of Council and a Trustee, because I still enjoy the Society and felt it would be fun to be involved, at least a little, in decision making.

But the Society has changed enormously. It was a Society primarily for giving abstracts and oral and poster presentations four times a year, which was the number of meetings I used to have to organise, because it took a long time to publish a paper in the 1980s. And now from acceptance to submission to acceptance to publication you can get something out in a couple of months. In those days it would sometimes take a year so people wanted to establish primacy of discovery by presenting to the BPS [British Pharmacological Society].

My very first oral presentation was actually to the Biochemical Society, who met at the Institute of Psychiatry down in Denmark Hill, and at the end I was asked a question about the levels of serotonin metabolites in the CSF [cerebrospinal fluid]. I, of course, was working just on rats and said that, ‘No I hadn’t done anything but there’d been some really interesting work going on by Ashcroft and Eccleston in Edinburgh studying that very thing.’ And after I had finished the person asking a question saying, ‘Thank you very much’ very politely, I went off to see my supervisor who said, ‘That was a nice presentation. And you know who asked that question?’ ‘No,’ I answered. ‘Ah,’ he said, ‘That was George Ashcroft.’ I was fairly mortified but Gerald [Curzon] pointed out that all scientists like their own work being quoted back at them.

### [4]. THE BRITISH ASSOCIATION FOR PSYCHOPHARMACOLOGY

I got involved in the British Association for Psychopharmacology very near its start, in 1974. It was started primarily by psychiatrists and they wanted a fairly closed shop, but there were considerable objections from people like Malcolm Lader, who is a clinician, and Philip Bradley, the Professor of Neuropharmacology in Birmingham. Actually, he was Professor of Pharmacology and Head of the MRC Neuropharmacology Unit. And as a result of a meeting in the November of that year, the Society became much more open, changed its title from the ‘British Academy’ to the ‘British Association’ and I joined, and I’ve been involved ever since through, again, being on their journal, the *Journal of Psychopharmacology*, on Council for a bit, and then coming back fairly recently by being a Member of the Governance Panel. So I’ve been involved with that, and it’s a really pleasant mix of both psychiatrists and basic scientists looking towards translating data backwards and forwards.

### [5]. THE SEROTONIN CLUB

In 1987 Paul Vanhoutte came to England, help set up the Serotonin Club. He decided that, rather like the Catecholamine Club and the Histamine Club, there should be a club of people interested in serotonin, which is really rather late when one thinks about it. And we met, I think, in the lecture theatre, anyone who was interested, at the School of Pharmacy, and he gave a talk about what he wanted to do and how he wanted

to set it up, and then I have to say, as far as I was concerned, totally out of the blue said, 'Well, Richard Green could be one of the British officers.' So, yes, thank you. I then moved on to being Vice President and President. I wasn't sure because I was right in the middle of my activities with Astra in those days, so I'm not sure that I was as active as I ought to have been as President, so when the job as Treasurer/Secretary came up, I said 'Yes I'd do that.' And I did that then for about 10 or 12 years I think, which was very enjoyable, because I had to write a newsletter and help, get involved in organising meetings. We always ran a meeting at Christmastime as a sort of offshoot of the British Pharmacological Society meeting, because a lot of people from Pat Humphrey to Danny Hoyer; there was a very strong serotonin research in the UK and Europe. John Fozard is another that should be mentioned.

So we always had a lecture and a dinner on one of the quieter evenings of the BPS meeting, so enormous fun. Recently, well I asked actually when I was Secretary whether we ought to change the name because 'Serotonin Club' sounded a bit informal when we were trying to get money to help support the meetings. And everyone, including Paul Vanhoutte, said 'No, they liked the name.'

A few years ago either started, or certainly supported, by Paul, a move was made to change, and the Society is now called the 'International Society for Serotonin Research', ISSR. There was a small movement to suggest it should be called the 'Society for Serotonin Research International', SSRI, a clever play on words of the serotonin selective antidepressant drugs, but I think that was a step too far.

## [6]. NEUROPHARMACOLOGY: ECT, AND RECREATIONAL DRUGS

Well, certainly what I'm proud of is the work that's been done in neuropharmacology, primarily I think linked with other good neuropharmacologists and psychiatrists within the UK. I've been fortunate in having some very top people working with me, often at the early end of their career. I mean obviously particularly I'd like to mention David Nutt, Phil Cowen and Guy Goodwin, three who went on to become major personalities in the British psychopharmacology scene. But in doing that I'm probably omitting, and I hope I don't offend them, a substantial number of other very senior people who I've had the privilege of working with, sometimes over fairly short periods because we've got together, decided we've got a joint interest in something. We've studied it, published it, and we moved on.

I think the work with David Grahame-Smith in Oxford, where we were looking at ways to measure 5-HT [5-hydroxytryptamine], serotonin function, in animals, with a view to understanding more how drugs work in psychiatric disorders, has been something that I'm particularly pleased with. And within that, I think, the work we did on ECT [electroconvulsive therapy], when people for years had been saying that ECT didn't have a specific mechanism of action, and we were able to show, at least in experimental animals, that if they got a series of electroconvulsive shocks under anaesthetic in very much the way that ECT is given to severe depressed patients, then there are very specific changes in the brain and those changes are certainly consistent with the way that some other antidepressants work. So we were seeing the same type of change occurring, and I think that gave a boost actually to psychiatrists to say there is a pharmacological type mechanism of action occurring. And I suspect partly as a result of that, Tim Crow and Eve Johnstone, who were at Northwick Park [Hospital], were able to do a clinical trial on whether ECT was efficacious and show that it was. And it gave a boost actually to the use of ECT in severe cases where no other treatments had been shown to be useful.

The other work that I've been much involved with from, gosh, the early 1990s right up to now has been studies on what are sometimes called 'recreational drugs', ecstasy in particular, mephedrone more recently, finding out perhaps a little of what they're doing and again how dangerous they are if young people take them. And trying again, in current terminology 'translation', between animals and humans and what to look out for. Because we know that people are not going to stop taking recreational drugs, it's embedded I think in mankind as you look into it. But at best perhaps, suggesting that young people, if they are going to take them, should think about how much they take, what else they take with them on the basis of animal work, has been pleasing. I mean people, young people, will continue to take these drugs. The more they're informed, I think, the more that they're able to make decisions as to how much they take, whether they mix

them with other drugs, and in that regard it's been quite interesting that I'm getting back to linking with my old colleague, David Nutt, who of course over the last few years has spent most of his professional life talking about relative risk of all these drugs. And you know we have talked about this and we've recently published on how research should be conducted on drugs, both pre-clinically and clinically, so we can believe in the results that we obtain.

#### [7]. WORK ON STROKE AND THE SHOCK OF FAILURE

I think thinking about things that go wrong, not very much really in terms of career because often things have happened by chance. I've linked with the right people and I've had a lot of fun. The one serious thing that went wrong is in working with Astra where we were doing work on neuroprotective drugs for stroke. We had an extremely good drug called NXY-059. We went right through from the basic work to the clinic, had one positive Phase 3 trial and the second one was totally negative, and the whole project stopped. That was very upsetting, not the least because you spent years on it but mainly because there was nothing available in this type of approach to stroke and we really thought we were going to be helping stroke patients and, even if we had a fairly modest improvement in terms of numbers, and we weren't aiming high, it meant that we were likely to be able to get some patients to lead a much better life. And the shock of failure in that was really quite considerable.

#### [8]. CHANGING TECHNIQUES

Major changes in my career. I always felt that when I did my PhD I was doing it using the techniques and the methods and approaches that were somewhat similar to those that my PhD supervisor had done. Okay, the equipment might be a bit better, but the overall approaches and the way we did things were very similar. There is no point now I have found with my recent students saying, 'Ah well, this is the way we did it,' because everything is so different. The technology is different, from mouth pipettes to the micro pipettes that we now use. Micro techniques often in terms of the amount of solution we use. I mean a very good example, I think, is that when I did my PhD I was able to use a mechanical calculator, and I then used to draw up a graph by hand; electronic calculators came about six or seven years later from that time and to me they seemed an enormous advance. We drew graphs by hand, we took them up to a department in the Hospital called the 'Department of Medical Illustration', who then used Letraset and fine pens and drew up the graphs beautifully. Once we'd approved them they would make photographs and we would stick them onto pieces of paper to send in with our manuscript. Now using GraphPad Prism I don't even have to calculate the data, all I do is put in raw data. It will do all the statistics for me. It will do the means, it will do the standard deviations, it will draw up the graphs, it will label it, I'll print it out and then I upload it on a webpage and that's what the journal takes. It is an enormous change actually.

#### [9]. INTEGRATIVE PHARMACOLOGY

I'm very much, I guess, what these days is called an 'integrative pharmacologist'. I know a few years ago when AstraZeneca were changing some people - were being really retired early - and I got a little worried about this and had my then boss, Christer Köhler say, 'I don't know why you're worried, I can pick up handfuls of molecular biologists, it's people that know what's going on in the whole animal that I'm short of, so you have great value.' And I've continued with that. I mean I like to know, if I give a drug, what it does to a variety of systems either in the brain or periphery. And I have to say some of the molecular biology has passed me by. As I go to the [British] Pharmacological Society meetings ever more passes me by, particularly as we get to the more genetic side of things. I mean that is the way, I'm sure, at least in psychopharmacology, things will be going ever more, I mean, sort of targeted drugs and individual drug therapy based on genetic information, I think will become much more major. But that is not going to stop the need for early studies both in the test tube and then into the whole animal. I remember David Grahame-Smith, who was my Prof in Oxford for 12-13 years and was on the Committee of the Safety of Medicines, saying to me one day, 'Well,' he said, 'you know, the thing is, in general we tend to assume that if a company is submitting a drug application they have got it right about what the drug will do. If they want a drug to target the 5-HT receptor, it's going to do that, because that's important to them. I tend to skip over that

part of information to some extent because they will have got that right. What I want to know is, if they're targeting a neuron in the brain, what that drug is doing in the liver and the kidney and everywhere else because,' he said finally, 'that's going to be a problem if the drug is going to produce a problem.' He said, 'We can always be experts at what we want to see, it's all the other systems.' And we've got to continue with integrative pharmacology for that reason, if nothing else.

[END OF TRANSCRIPT]

**Further related resources:**

1. Overy C, Tansey E M (eds) (2013) *Drugs Affecting 5-HT Systems*. Wellcome Witnesses to Contemporary Medicine, vol. 47. London: Queen Mary, University of London.
2. Tansey E M (intvr); Tansey E M, Zarros A (eds) (2016) *Green, Richard: transcript of an audio interview (17-Dec-2015)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016034. London: Queen Mary University of London.