An interview with John S. Gillespie

Conducted by David J. Miller with Martin Rosenberg and Tom C. Muir
on 1 March 2006

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The Physiological Society

John Gillespie photographed by Martin Rosenberg in 2006.

John Gillespie (1926–2009) was distinguished for his pioneering work on what was long known as "non-adrenergic non-cholinergic" neurotransmission in smooth muscle. His work helped build the foundations for the discovery of nitric oxide as a neurotransmitter and thus for better understanding the control of smooth muscle function and nitrergic nerve functions. He was also a highly skilled and respected strategic thinker and administrator. He was the founding Professor of Pharmacology at Glasgow University where he later served (twice) as Vice Principal. He chaired MRC grants committees and became a Fellow of the Royal Society of Edinburgh in 1979. For The Physiological Society, John was elected a member in 1957; he served on the Editorial Board of Monographs and was Meetings Secretary (1966–69) and Committee Secretary (1969–72). He became an Honorary Member in 1992.

This interview was conducted in the West Medical Building, Univerity of Glasgow, 1 March 2006. Those contributing were: John Gillespie (JSG), David Miller (DJM), Tom Muir (TCM) and Martin Rosenberg (MR).

DJM: To get us started, could you just tell us a little about your family background and your early education, possibly with a hint of how you've ended up where you are, in physiology and pharmacology?

JSG: Sure, my family background would be essentially a working class background. My education would be mainly during the Second World War; well it was much interrupted by the Blitz and by the evacuation and so on. But even before that time I had decided – although I'd never mentioned to anybody – that what I wanted to do was to be a doctor. I think this really stems from long periods I spent in hospital; I *think* that must have influenced me, certainly. Even in primary school I was determined that's what I would become. So, eventually I went on to take the Highers [final examinations in Scottish secondary schools] and sit the bursary competition and get a position in the Glasgow [University] Medical School and then to qualify in medicine.

DJM: Do you have any siblings who had similar aims?

JSG: Yes I have a brother and sister who are both now dead; I was the youngest in the family. My brother ended up in Australia, as many people did at that time.

DJM: So were you the first in your family to have received a university education?

JSG: Oh yes, undoubtedly. I would have been regarded in the group that I [was] brought up with as most unusual. I don't think anybody had ever gone to university, not just in my family, but also from anywhere near where I lived.

DJM: Do you recollect being sponsored or supported by, say, a particular schoolteacher or perhaps one of your parents? Did you feel it was working that way for you?

JSG: Not really. I mean I was in so many schools, many of them for half time or for six months off, but in the end I ended up in Dumbarton Academy that I reckon was a good school. I felt it prepared me well for what was needed for the Highers and for the Bursary Competition. I can't really remember any particular teacher as being an outstanding influence on me. Already at that stage, I and a friend, Archie Douglas – who eventually became Professor of Geology down in Newcastle – we were both extremely interested in science. So, as young children, we spent our time trying to make microscopes, find the bits to make microscopes or doing chemistry experiments at home and so on. I think that kind of interest plays in some ways a bigger part in directing your future than formal education.

TCM: Was your choice of Medicine in any way influenced by the fact that Scots were at that time very well known to produce ministers, doctors and engineers?

JSG: No not at all, I mean I don't know that I would have even known that at that stage when I'd made the decision. I think it would have been influenced by the young Houseman I met in the Sick Kid's Hospital, and yes, a personal influence with these people.

TCM: Was there a home influence in directing you towards Medicine?

JSG: No, there would be endless support but there would be no home influence. Given the sort of social background I was in, the information needed to do that was not really available. People didn't know what they needed to do to get into university: I myself, for instance, when it came to filling in the application to get into university which would now be the UCAS form. I was convinced – and thought this until the Headmaster corrected me – that I wished to take the degree of MD because all the books I had ever read were by people with the title MD, so that's what I thought!

DJM: So then, do you want to go through how your undergraduate time developed?

JSG: Yes, sure and this would be just an account of wee bits of what I felt about physiology. 1945 was my first acquaintance with physiology as a second year medical student. In those days, unlike today, in the second year we'd only two courses, Physiology and Anatomy, although Physiology had lost Psychology quite recently as a block – Physiology has constantly lost bits of subject matter. The professor here then was Cathcart [E. P. Cathcart, 1877–1954, Regius Professor of Physiology, Glasgow University]; it was his last year when I was there – he still gave lecturers in psychology on Saturday mornings which many of us attended. Physiology still was made up of experimental physiology, as we would know it, biochemistry and histology; they were all pretty equal then.

Coming into the Department, the experimental physiology (which I think I should stick to, more or less), was very much dominated by the smoked drum. In those days, there was a great shaft which ran down the long benches with a motor at one end and a shaft. Then there were pulleys at each student's place driving a six-inch smoke drum. I have kept my lecture notes and my laboratory notes from these days (and I was just looking through them) and it was a pretty good course of what we knew at the time. In the practical classes we used the pithed frog**;** we studied the genesis of tetanus in muscle, the Stannius ligature and so on in the heart, all these old experiments. We did a great deal of human physiology measuring nearly everything you could; haemoglobin, lung volumes, blood pressure – all of that sort of stuff was done in the course. But the equipment was very primitive, not like that today. It was the small smoke drum, induction coils to stimulate nerves; I see one there [in the interview room] which is from the class. We got our 4 volts from big submarine batteries at the end of the bench. I must say I enjoyed that course enormously. It certainly interested me. Then I ran away and did my Houseman jobs, did my couple of years in the Army in National Service, came back and did a year in hospital again.

Then, in 1952, I thought I would come back to physiology and get some experience of research, give a couple of years to research and then go back to hospital medicine. It's interesting to remember that there was very little research that we would understand [today] with [poorly equipped] laboratories in the hospitals in those days. People who wanted to do experimental work would come to the Physiology Department; some of them went to the Anatomy Department when that was appropriate. So, at that time, departments like Physiology were essentially medical departments. I was going to read a wee bit I've got from a few of these letters. This one from [Professor Robert C.] Garry which he wrote to me; the letter was mainly about Peter [*sic*] Gilding [Henry Percy Gilding, 1895–1973] writing the history of The Society. I'll miss that out, but I will come to a wee bit at the end where he says;

Here is another anecdote for your collection, John, from Willie Bain [W. A. Bain, 1905–71]: two applicants for the Chair of Physiology at University College Dundee in 1935. They were interviewed in the Senate Room of St Andrews; Willie went in first and he was powerfully backed by Dale, [Sharpey-]Schafer and McSwiney …

McSwiney was a powerful man in those days [B. A. McSwiney FRS, d. 1947]. Of [Sharpey-]Schafer, Garry says he had dropped the umlaut by this time from his name. He says that:

Willie Bain was the brightest boy he ever had. "So good luck," said Willie as I went in next and Garry got the chair. Piggy Charteris said to me subsequently, "Only your medical degree gave you the chair in Dundee. The Medical Faculty wasn't prepared to have a non-medical in Dundee; had it been the St Andrews chair it would have been a different story." [F. J. Charteris; he had lectured at Glasgow and, in 1919, became Prof of Materia Medica at St Andrews University.]

So in those days it was a very much a medical subject that we had here. Anyway, I came back here and I was absolutely seduced by experimental physiology at that time, I thought it was marvellous, I really did. It was an absolute pleasure to come in every day to the lab and to do experimental work. The lab hadn't changed in these years from '45 to '52. The teaching lab, for medical students in particular, was unchanged. What I don't think any of us realised then was that that era – the '50s to '60s – was really the high point and the end of a very sophisticated technology based on the smoked drum. When people speak of the smoked drum now they regard it as a very quaint, strange anachronism they couldn't understand, but in fact it was an extremely sophisticated system. It was not only that the drums themselves – I went from the 6 inch drum and then I went to this, which is the 10 inch drum – then I get an extension kymograph. And then somebody must have been very good to me and gave me the machinery that was the Brodie–Starling smoked drum. Associated with that were the most elegant levers, piston recorders, volume recorders – all sorts of sophisticated apparatus that has disappeared completely now, of course. It was quite interesting. I had gone to University College to work with G.L. [Brown] for a year or two and came back to Glasgow when I got the [Royal Society] Sophie Frick Research Fellowship to go to the Rockefeller Institute, which it was then: that was in 1960. It was not very long [after my time in London] and that was a revelation: there wasn't a single smoked drum in the whole of the Institute, nobody knew about the smoked drum. By then it was oscilloscopes and Grass pen recorders, whilst the smoked drum and all the equipment ancillary to it had been dominated by Palmer [& Co.] in this country. Once we went to this new apparatus, the whole pen recorder thing was then, and I think still possibly is now, dominated by Grass, [which was run by] Dr Grass and his wife Helen. God, she was a terrible woman: she would terrify you even on the telephone. Helen Grass could terrify *me* even on the telephone!

MR: And they wouldn't give you their circuit details and all the wires were the same colour!

JSG: Eventually, I took a lot of the equipment back here [to the UK] and wanted some additional stuff. I phoned up America and Helen was on to you immediately. Her records were up quickly and she knew exactly what I had, why I was asking for the wrong thing and she would put me right. Dr Grass, of course, he did the actual designing of the equipment and had nothing to do with the running [of the business], but their equipment was the thing which was then dominant and I expect that maybe it still is.

TCM: It's been taken over now I think.

JSG: Oh has it? Well [Dr Grass] must be dead.

TCM: I remember a story when asking for a bit of equipment; an isolation box that didn't have a stimulator to match and she said, "you do not have that, you should order it!"

JSG: Yes so it was quite a thing to get your spirits up to phone up Helen Grass! One of the things I thought – and maybe it's just because I'm too old now and taken aback about things but I think this [marked a] change – before this, all of us were well acquainted with the apparatus. Some of it we made ourselves. We really were expected, then, to be able to do all sorts of other technology, to photograph things, to mount traces. In those days *The Journal of Physiology* insisted that you sent them the original traces before they would publish anything. You could send them a photograph for the referee to work from, but they insisted on the original traces. What used to infuriate me was that they would always change my labelling to their own when the thing finally would appear. All that, of course, was going to disappear and I think has disappeared. I may be unfair, but I guess nowadays maybe research workers use almost nothing but industrially produced equipment; very complex, very expensive and very necessary if you want to keep up with the sharp end. But

I think that's had quite an effect, both on teaching students and on research. In terms of teaching students, it used to be quite cheap being able to teach an Honours student. But if you wanted to teach them with modern equipment, it became very expensive and in the end, [so did] the research projects, the elaborate laboratory work, as Tom [Muir] used to teach them on how to use microelectrodes, single cell recording; all that was going to disappear because the equipment was too expense for that sort of thing. I have a feeling that maybe in research … it is no longer possible for somebody to have his own ideas and get started on simple equipment. You really need to join a group and get started in the group and that will probably define the things you go on working in because it has a very big influence on you when you start out. So that was all I was going to say about such things as I could remember about physiology.

DJM: If I could just inject a question there John. You mentioned the idea that you decided to come back to the Physiology lab to do some research, so at that time were you intending to do a PhD? Was that regarded as the necessary component?

JSG: No I don't think when I came back I had the PhD necessarily in mind because I was thinking a couple of years [research] and I would go back [to medicine]. I really wanted to find out something about research methodology.

DJM: So you saw using that time to inform you better as a doctor in the future?

JSG: That's right. At that time, as I said, physiology was a very medical subject and what was taught down there in the Lecture Theatre had very medically orientated aspects to it. I really felt that a lot of medicine was founded in physiology and that's where I should acquire the skills if I wanted to be involved in clinical medicine and clinical research. But I very quickly changed my mind and then, of course, a PhD would be what I was going to do.

TCM: What led to your interest in the electrical recording?

JG Well I will come back to that, it was really ...

TCM: Was it University College [London]?

JSG: No it was simply that I had earlier on produced that preparation of the rabbit colon with a double pelvic sympathetic and parasympathetic innervation. Just a year or so before, Edith Bulbring had been the first to record [spontaneous] electrical activity from the single cells in the taenia coli. I felt that the rabbit colon would be a good preparation to allow me to record the effects of both sympathetic and parasympathetic stimulation and so that's what took me – and knowing that I was going to the Rockefeller to do that, I went down to work with Otto … and there I was introduced to single cell recording and cardiac muscle.

MR: Otto Hutter?

JSG: Yes. Otto Hutter, from whom I gained the information on microelectrodes, how to make them, how to record from them and so on.

DJM: And just one last point about your decision to come and taste a bit of research, how was that funded? I mean in what guise were you funded then to be here working?

JSG Oh I was a research scholar, there was a research scholarship available.

DJM: Available to medical students?

JSG: Yeah.

DJM: Good.

JSG: So, to the Phy Soc; yes I think I will say something about my memories and maybe others I've mentioned before talking about what it was like around about '52 when I came back into the Physiology Department here. At that time, Society membership was really quite restricted. The numbers being admitted every year was a thing for the Society to decide. It was regarded as a highly privileged thing to be a member of The Physiological Society. We even had A. V. Hill, I remember, calculating in those elaborate ways he could do, all accounting for deaths and so on, the number coming in to physiology that we should elect every year; I don't think we ever did it. It was very much, as my memory goes, it was very much like a gentleman's club and for that reason nearly everyone there was older [than me]; it seemed to me a [group of] older established physiologists and there was only a handful of young PhDs or people doing an assistant lectureship who would be at these meetings. It was really pretty terrifying but mostly embarrassing, you know. All these old boys went there to have a chat with their friends and the dominant times were tea times in the lab, always there in the one of the big labs. And then the Dinner; if you really knew nobody tea time or Dinner time, it was quite a strain, I thought. The Society was very fair but it could be quite savage with Communications. At that time, people were quite nervous about giving their Communication to The Physiological Society.

The Demonstrations: In those days, there would maybe only be six, eight, maybe 10 demonstrations. There wasn't a great mass of Demonstrations and of course there were no Poster Communications. The demonstrations were real experiments, very tremendous experiments, that people would do. Whichever Department you had gone to visit, they would put on a Demonstration of their own experimental work that they were doing in their own laboratory. If you were a visitor giving a demonstration, you would usually do that in one of the advanced teaching laboratories. You would often take all of your own equipment down. The first Demonstration I gave was in '54 at Mill Hill (up from where you are coming from Martin).

MR: Yes.

JSG: There was a meeting every year in Mill Hill in November. I was going to demonstrate this doubly innervated rabbit colon preparation and as a result of this we took down all the organ baths, stimulators, keys, everything that was needed, except the rabbit! I can remember that particular demonstration so well. I don't know what the position is now, but in those days for a Demonstration you were allowed 5 minutes in the lecture theatre to tell people what you were going to show them and you were allowed to show one slide. So I got up and gave them my wee talk and showed them my one slide. But since I had a rabbit to dissect, I walked straight out the lecture theatre and I was down below there dissecting away and about 5 or 10 minutes later Garry, who I was working with, Professor Garry here, came in and was like "*urggghhh I'll fight it, I'll fight it*". After I could get some sense from him, it turned out that Feldberg had challenged him in the description we had given. In those days – and I was looking at my [student] notes and that's where I was taught that the term "sympathetic nervous system" was still used for the whole autonomic nervous system. The *Encyclopaedia Britannica* still had the whole thing described under "the sympathetic nervous system" and from my lecture notes I see I still had it under the sympathetic nervous system. So, [to distinguish the two divisions] we had called it the effects on the rabbit colon of stimulating the ortho-sympathetic and the parasympathetic. He (Feldberg) was quite right and that [labelling] never lasted in the full paper; we certainly cut it out. So that was the way The Society looked to me as a young member just going down to the meetings.

In 1957 I was elected a member of The Society and then in 1965 I was elected to the Committee. Then in '66, I was elected Honorary Secretary and, as I think it probably still is today, you spent 3 years as Meetings Secretary and 3 years Committee Secretary; I think that's still probably the same. It was a very informal business. [As to] The Society organisation then, we had no President. We took great pride in having no President – unlike the Anatomical Society which had a very long chain of Presidents. What we had was this, the Brown Dog. One of the functions of the Meetings Secretary was to take this to every meeting where it went in front of the Chairman at Dinner. One of the things which the Meetings Secretary would worry about, or remember after a few glasses of wine, was to lift this damn thing and take it back home with them. Only once did I fail to do it and again that was in Mill Hill. Although we had no President, we did elect a Chairman of the Committee. One of the rules was that, if he didn't turn up within 5 minutes of the start of the meeting, we would elect a new one, for that meeting only. This, of course, is not the original Dog which I believe we've lost.

DJM: Yes stolen from the back of Reg Chapman's car when he was Secretary. [For the story of the dog, see http://bit.ly/1izZsso.]

JSG: I will give you a wee story; this is a copy of the Dog in bronze. It was ordered by Eric Denton – Eric Denton got six of these made; he kept one, I've got one, George Bell got one [Reg Chapman two], and I don't know what happened to the other [one]. He had it cast by the same people who cast Henry Moore's bronzes so it's probably a good casting. A man had a look at it to decide how to split it so that you do this kind of thing. After he looked at it for some time he said, "You will be doing this for sentimental reasons." So I don't think he ever thought it was a great object as an *animalia* bronze.

The Meetings Secretary was a bigger problem. I mean, it was more work than being the Committee Secretary. The main thing was to organise the meetings; we had nine of them each year. Some of them were fixed every year; we had a March meeting in University College, we had a July meeting in Oxford or Cambridge and we had a November meeting always in Mill Hill and the rest then were scattered around the country. There would be a meeting in Scotland once a year and so on; we just scattered these around [on the invitation of the Heads of Departments].

When the meeting was in Cambridge in July there was also a meeting in Babraham and that gave the Meetings Secretary terrible trouble because Bryan Matthews hated having the meeting in Babraham on the morning of the Friday. Therefore, he used to grab the Meetings Secretary and insist that he made sure everyone was out of Babraham – and back there in Cambridge – in time for the 2 o'clock start. Knowing the bunch of physiologists, it was not easy for the Meetings Secretary to get them all moving in time for that. Often in those days there were not a lot of communications. To begin with, they might all have been in the one lecture theatre. That had a really great advantage in that the physiologists heard a whole range of subjects. Everyone who went down to give a paper got the benefit of the advice and comments of very senior people, Huxley, Hodgkin, Bernard Katz [and Henry Dale] – they had all sorts of senior people there who would contribute to the discussion. I thought that was very useful to the people giving the paper. The Meetings Secretary used to have to sit there and listen to all the papers and make notes of any changes that were required before the paper was accepted. Of course, it was all voted on [then]; it might be voted out. The other thing the Meetings Secretary was to do was to write up the Minutes, but that wasn't a big task because you could do it from home. But you had to read the Minutes at the next meeting.

The worst job for the Meetings Secretary was to get somebody to propose the vote of thanks after the Dinner. If that was not done in advance, you had to do that at teatime. The Meetings Secretary used teatime to put the black spot on somebody to give the vote of thanks. At teatime, the Meetings Secretary had absolutely no friends; you could go up to any group and it would just melt away, disappear.

MR: What was the worst response you got?

JG Oh I won't get into that.

MR: Or what was the best response?

JG I will tell you the best response I got. The best response – and I can't remember where I was; I think it might have been Oxford. Anyway, I hadn't got anybody to give the reply and I didn't remember that I was in that position until the Chairman was up there giving his normal thanks to his secretary, to the technicians and everybody who assisted in the meeting except himself. He was in the middle of this when I suddenly realised, gosh, I haven't got anybody to do the vote of thanks. And I say to his great credit, I was sitting next to David Whitteridge. David was a man to whom somebody had applied the phrase "Whitteridge is of high IQ but low pH". I asked Whitteridge would he do it, and he did it on the spot. That was a noble act, I can tell you.

Then I went on to become Committee Secretary which was an easier job altogether. Most of time we were concerned with membership, with finance, with the links with physiologists abroad and intermittently with problems with the Home Office. At an earlier stage, there was a big change in the law about animal experimentation and proposals had been circulated to all the appropriate societies; we had to reply to that. I do remember one thing, that they had omitted the decerebrate animal and anaesthetisation for all experimental animals and we had to correct that particular bit.

On the finance side of things, it was quite interesting; it was just about this period that The Society started to get rich. It hadn't been rich before, but *The Journal of Physiology* was being taken much more widely. There were more Physiology Departments worldwide and the income to The Society was increasing quite noticeably. There was a bit of a discussion as to what we should do with this money. I was in very much for keeping it; a good Scottish view of things.

At that time, the total income from *The Journal* was £72,000 a year, I think. It seemed to me that we should have at least that amount of capital put by in case something happened to *The Journal*, but the main proponent of the opposite view was Andrew Huxley. Andrew believed that the whole purpose of The Society was to support physiology; what were we doing accumulating cash? We should be spending it supporting projects and supporting young physiologists and not accumulate this cash; we did accumulate the cash, as it happened!

Another thing that comes to mind is Norrie Vass. Do you remember Norrie?

MR: Oh yes.

JSG: Norrie Vass was a permanent member of the Committee because he represented International Abstracts. At that time, we were beginning to realise that the *International Abstracts of Biological Science* were really no longer serving a very great purpose, [but] we were supporting it financially quite considerably. *International Abstracts* was produced by Pergamon Press, under the late 'Captain' Bob Maxwell. Maxwell had both a powerful personality but then an extremely charming personality – I never met him, but I'm assured of that. Every year, Norrie Vass would go up and be challenged by Bob Maxwell on whether it really was worth keeping these, were they important things that should be kept? Then Norrie would come back and charm the Committee in continuing and was successful for several years. But eventually we abandoned the *International Abstracts* and dropped it.

At this time too, one of the things I did do was to produce a pamphlet for schools: *Physiology as an Education & Career*. I stole the title from A. V. Hill; he had given a lecture – I think it must have been one of the [Royal Institution] Christmas Lectures or something similar. It seemed a good title to me, so I used this. When we had produced eight or nine thousand, we then sent this pamphlet to every school in the United Kingdom to the careers guidance teachers. I doubt if it ever did any good in recruiting physiologists to be truthful, but it was quite interesting to do.

DJM: With colour photographs, as I remember?

JSG: Yes it had colour photographs.

DJM: With that strange cartoon of the axon and the squid on the front?

JSG: That was my production.

DJM: It had an effect on me then.

JSG: One of the things which is quite difficult, as I would find it … Everybody knew then J. Z. Young's discovery of the squid axon and Hodgkin, Huxley had done their work with Bernard Katz and so on. The squid axon was very well known, but what I found almost impossible to find out – even from a zoologist – is how the endings appeared in the muscle so there is a certain amount of ambiguity when you get to the end of that particular cartoon.

I'd come into research, and I think the first thing to say is that I started in 1952 and ended in 1992 working on the same topic; it surprised me. When I came into the Department, Garry wanted me to work on a project that stemmed from Langley – Langley and Anderson 1895, 1896 and 1897. Langley would be for me a hero of physiology but I know he would have disliked me and I would have disliked him intensely if I'd ever met him. He was described by Josh Burn as "of mad blue eyes and rode to hounds"! But he was a superb experimenter. If Langley has ever said that he saw something then he saw it and it's true. He worked, as you will see later from a wee thing I'm going to read, on very simple equipment. He did do some smoked drum work, but mainly he worked with a microscope, a magnifying glass and dissecting instruments. He said that if he "saw something with his own eyes" he could believe it, "but an instrument might be misleading him".

Anyway, the thing that started me was that he had done work on the effects of stimulating the vagus and the sympathetic nerves in a whole variety of tissues. This was the time when he established the [modern] nomenclature**,** what Gaskell called the "vegetative nervous system" that would now become the autonomic nervous system. The two divisions would have been sympathetic and the parasympathetic and it was Langley who established that neatly. He was looking at the effects of stimulating sympathetic and parasympathetic in many tissues. The interesting one is when he stimulated the vagus to the stomach it nearly always caused the stomach to contract. But occasionally, it would relax and it was not clear why this was so. The problem was worked on in the 1920s and '30s by various people, amongst them McSwiney and indeed by Brown and Garry in Leeds, but there was never an answer to it. So the problem that was given to me by Garry was to see if, instead of the cranial parasympathetic vagus, we stimulated the sacral parasympathetic, the pelvic nerve and looked at the colon, would we find that, there too, you could get contraction most of time, but occasionally relaxation. So that was the project. We set up an isolated preparation of the rabbit colon in which we could stimulate the sympathetic and parasympathetic. I had great guidance from the dissections that Langley had published in these three articles where he dissected various animals: cat and the rabbit. He had dissected the pelvic plexus; he had done it beautifully. A beautiful dissection. So we worked on that and that's the thing I took down to Mill Hill as my first demonstration. The outcome was that, when you stimulated the pelvic, it was always contraction; under no circumstances would you get relaxation. If you stimulated the sympathetic it always relaxed. There was a difference in the frequency sensitivity, so if you mixed them, you could pick one or the other. We thought this meant that the other work in the vagus – that it was a mixed nerve – and that would be the explanation.

That was the end of that particular project at that time. Because Garry and G. L. Brown had worked together in Leeds and were great friends, it was arranged that I would go down to University College London as the Faulds Fellow. I remember the work but, at the time, it didn't look like an awful exciting project. It was known that if you use different frequencies you could cause the action potential in the nerve to get bigger, sometimes referred to as postsynaptic enhancement and sometimes Wedensky inhibition – those were all phrases used. G.L. had worked on this and demonstrated the increase with Oliver Holmes, who also used to work here [in Glasgow]. That was the thing they did and so my project was: when that bigger action potential arrived at the nerve ending would it release more transmitter? The idea was that I was able to measure noradrenaline coming from nerves and – if we arranged to get the bigger action potentials – would we get more transmitter?

First I had to go to Edinburgh for a couple of months and work with Marthe Vogt on how to measure noradrenaline on the rat's blood pressure and how to separate adrenaline and noradrenaline using paper chromatography; big paper chromatography in great big tanks**.** When I got down to London to University College, the atmosphere there was really quite different from Glasgow. It was very much more active in terms of research. That's not surprising because there were so many very distinguished people there in the related departments not just G. L. [Brown] but John Gray was there, J. Z. Young was there, Bernard Katz was there, Paul Fatt – there were lots of distinguished people there. Hugh Davson, who I believe you have recorded, was there too. I liked Hugh; he was a very intellectual man.

Anyway, it was a different kind of atmosphere altogether and we had quite a few overseas workers who came and worked – Mel Schachter and people like that. In those days, it was quite normal that you would be expected to do some teaching and that relieved the local people who had more time for their research, so it was quite fair. Thus it was in University College that I gave my first big block of lectures to medical students: I did the block on respiration.

MR: What year was that?

JSG: Well it must have been 1956, yes 1956. I would give that, it was quite a big block of lectures probably the best lectures I ever gave, I suspect.

MR: In the Physiology Theatre?

JSG: Yes in the Physiology Lecture Theatre. It was great fun at University College. G.L. and I got on extremely well. I really had a kind of father and son relationship, I think, with G.L. He endured even me wiring up an Anglepoise lamp and I must have wired it up wrong because he just put his hand on it and was thrown back onto the floor – nearly electrocuted – but nevertheless he didn't take amiss.

MR: The chair didn't become vacant or anything like that!

JSG: No the chair did *not* become vacant, nor did he take it badly.

MR: Jim Pascoe was there wasn't he?

JSG: Jim Pascoe was there.

MR: He was my supervisor.

JSG: Oh was he? Oh yes, well Jim was there. There were all sorts of activities went on with students and with the staff. It happened before I got there, so it's nothing to do with me, but then they had become very interested in Highland Dancing. So, they had sessions of Highland Dancing during the week in the evening, especially on a Friday evening, either in the Staff Common Room or sometimes even in the Lecture Theatre. My memory is for G.L. it was "Strip the Willow"; that was his great favourite.

MR: Were you able to instruct?

JSG: No I was not, I mean, I knew how to do stuff but by the time I got there, it had been long established. Every week G.L. did an experiment with me – he did one experiment a week. Yet, at this time he was Biological Secretary of the Royal Society, so he was a busy man and it was good. He would always make a wee offering of rice to a god, an unknown god. It was penned at the back of the door of the laboratory. When we were working, if things went wrong and occasionally they did, he would curse away in Portuguese, which he had picked up when he had worked in Portugal on goats, and he would curse away like this. On the other hand, if it was an experiment that went extremely well, then there would be sherry in the lab. There was no health and safety stuff then; it would be sherry in the lab at the end of the day.

The first three months I was there and I didn't feel stressed as I remember it. I could have been, I suppose, as in that time I went through a whole lot of different tissues, cat colon, cat liver and so on, stimulating the hepatic nerve, I couldn't get any noradrenaline in the blood, couldn't get anything to measure. There's a famous experiment by Finkelbaum – you know how Loewi established *Vagusstoff* – and the equivalent experiment was one on the intestine by a man called Finkelbaum who stimulated sympathetic nerve to a wee bit of intestine and that flowed over and inhibited another bit of intestine. I don't think anybody has been able to reproduce that experiment. However, I couldn't get any and so finally I went to the cat spleen and that always worked well and we got a lovely overflow of noradrenaline that we could measure. But one of the problems with contraction of the spleen is the change in flow rate and there was a physiologist – I've lost my physiology book since, so I can't quite get his name – but he was an Austrian [probably Georg Hertting, University of Vienna, b. 1925] who argued that the changes were really all to do with flow rate, and that's where the serendipity came into it because we decided to abolish contraction by putting in dibenamine as it was then which is a powerful alpha blocking agent which prevented vasoconstriction. When you did that we got an enormous increase in the amount of transmitter and what was more important was that before that without dibenamine when we stimulated at low frequencies we would get very little but when we went to the higher frequencies we got a lot and we thought that was the postsynaptic enhancement. But when we put in the dibenamine the low frequency jumped up and the output transmitter was absolutely uniform of all frequencies and that made us go for a quite different explanation. We gave the wrong explanation … most of the time in my life in fact I have given the wrong explanation; I hope my experiments have always been right but the explanations at the time were based on the work of a physiologist called Supancic who had been working on the motor end plate and of course if you denervate skeletal muscle the cholinergic receptors begin to move out from the end plate. But cholinesterase that is concentrated at the end plate moves out at the same time. And that led to Supancic to make the suggestion that cholinesterase was the receptor and that's why they moved out together from the denervated nerve ending. We picked up on that and said if the cholinesterase could possibly be the [cholinergic] receptor perhaps the receptor for noradrenaline also destroys noradrenaline and that's what we had abolished with the dibenamine alpha receptor blocker. Of course that was wrong. It could only have been two years later that we had an international congress on catecholamines; Bill Paton [Sir William Drummond Macdonald Paton, 1917–1993] made the suggestion from work they were doing in the adrenal glands that, "no, it was because noradrenaline from the nerve endings was taken back into the [same noradrenergic] nerve endings", the first suggestion of re-uptake, and when we went to high frequencies it was coming out so quickly it was too fast for re-uptake [noradrenergic] mechanism and that's why we recovered it. Axelrod who was at that meeting went back to America and of course he had the radioactive noradrenaline and with which he was able in the mouse to demonstrate that there was re-uptake of noradrenaline into nerve endings.

So when I finished there at University College, I came back to Glasgow I think for about two years maybe and then I got this Sophie Frick research fellowship to go to the Rockefeller and at that point I was going back to the original work I had done with the rabbit colon. I was hoping to do microelectrode recording and that worked and we got the first record I think of the response to both sympathetic and parasympathetic nerves stimulation of smooth muscle. Then I come back here and the next few years I was involved and interested in noradrenaline uptake and by that time I was also interested in extra-neuronal uptake, the actual uptake into smooth muscle especially and in particular and I had taken up a microscopic technique described by Falck in Sweden [Bengt Falck and Nils-Åke Hillarp], the fluorescence technique, which allowed you to visualise adrenergic nerves – and they really were beautiful in the microscope, a beautiful sight the adrenergic nerves. And so I was working away in this sort of thing and a young medical man probably thinking and doing what I had original thought of doing came to work for a year. Gavin Maxwell, do any of you remember Gavin Maxwell? Anyway, he was a young man, young medic. He wanted to go back to medicine after a year, so I had to give him some sort of project that I thought would be sure to work so he could get something before he left. So I suggested he should use the microscope – fluorescence microscopy – to look at different layers in the gut and in particular to see if we could see the sphincters in the pylorus and the internal anal sphincter. These should have been innervated by adrenergic nerves to let them close and he did that. He had reported there were narrow bands with beautiful adrenergic endings in both places – and he was quite right – in the pylorus there it was. But if you look very closely at this sphincter in the colon, you could see there was serosa between adrenergic innervated muscle and the wall of the colon and that the muscle was not a bit of the colon; it was a separate muscle. So when we then did a careful dissection, I came across the anococcygeus muscle which is a beautiful wee muscle, 3 or 4 cm long bilateral, which meant you could compare. It was very thin, it was beautifully innervated by adrenergic nerves and, if you stimulated it, you could show these adrenergic nerves produced contraction, and it was all characteristic of adrenergic nerves could be blocked by blocking agents and so on. But if you raised the tone in this muscle and then stimulated it, you got a powerful inhibition and that relaxation could not be blocked by either a sympathetic or parasympathetic – that is adrenergic or cholinergic – blocking drug. That I think that was the first clear demonstration of the things which Langley had reported earlier in the 1890s of non-adrenergic and non-cholinergic nerves except in the vagus they were mixed with motor fibres but in the pelvic nerve – as it went to the anococcygeus – there were no motor fibres but pure inhibition.

It was at that point that I began to look at other muscles; I would flip right back to where I first started in 1952 because in my thesis I had used a photograph of Langley's dissection of the rabbit taken in the 1896 paper. There was the equivalent of the anococcygeus muscle which he called caudo-anal and when I went to study them it was exactly the same, filled with the same fibres and I could have seen exactly what I was looking for [in 1952] in that muscle which was then millimetres from where I was dissecting. Of course that went on to be the inhibitory factor in nitric oxide; no I will not say any more than that … except that what I said was wrong. I was sure that it was going to be something different and a substance that you could store in granules and release them in the normal way with calcium entry and so on, but it turned out to be nitric oxide which you made on demand with entry of calcium, so I got that wrong.

I was going to give you a bit more on Cambridge and then Langley. I was going to start this by reading a thing here which hopefully won't take too long: this was something which A. V. Hill had sent to me, I sent on a copy to Garry and Garry says he was most interested in Orbeli's [Leon Orbeli, 1882–1958] memories of his time in Cambridge. He met Orbeli at the International Congress in Oxford in 1947 and he was there from the Russian Academy along with other Russians and, under the charge of a commissar, they were very reluctant to speak and very reluctant to appear be on friendly terms with physiologists from outside Russia. So when the commissar left the room immediately Orbeli shot across the room and said to me, *"You are from Glasgow? Do you know my old friend Cathcart? Is he here? Is he* *well?"* I had to say that Cathcart was not in Oxford: he had had a coronary thrombosis but was improving steadily. That was Garry's reply to a copy I sent him of the letter from A. V. Hill. The letter from A. V. Hill is addressed to "Dear Douglas", and I think that must be Douglas of the Douglas bag, and there he says:

A year or so ago I received from Russia a book containing Orbeli's reminisces. Not being able to read Russian I gave it to Caroline Humphrey, John Humphrey's daughter-in-law, wife of Nick.

That Humphreys lot is entwined with physiology and there are two different spellings to that name which was marvellous if you were Secretary of The Society**.**

She found that it contained a wonderful account of Cambridge 1909–1910 when Orbeli came here for a year and being a gifted linguistic Scholar she said she would translate it for me. She has made nearly a verbal translation, that is she has not turned it into formal English.

So it sounds kind of interestingly odd. Then he goes on to say people he has shown it to think it should certainly be published. He would like to publish it at the Cambridge meeting of The Physiological Society next July. I don't know if it ever was published, I somehow think it wasn't.

MR: Good to have it on record though?

JSG: I won't go into that … where else he might do it. So here is the memories of the Physiological Laboratory in Cambridge in 1909 to 1910 by Orbeli. Now A. V. Hill has got a couple of wee bits here, two paragraphs; I don't think there is anything really there I need to read so I will go onto Orbeli's thing:

In England I saw a completely different way of working. When I arrived I spent a few days in London and then went to see Cathcart in Glasgow. At some time or other he had visited Ivan Pavlov and had asked that we should drop in on him and so I thought it would be a good idea to accept his invitation, first in order only to orientate myself in English customs. [Goodness! In Glasgow!] In Glasgow I arrived, put up in a hotel and telephoned him; in 20 minutes or so he was already with me in the hotel, took all my things and conducted me to his home – I was his guest for three days. He lived with his mother, an old woman; she put me up for the nights in her own room making a bed for herself somewhere else. When I got into bed on the first night I gave a jump: under the blankets there was a bottle filled with hot water; that's the way they're accustomed to warm their feet.

Cathcart gave me many valuable pieces of advice. Having arrived with a beard he said it would be quite wrong to have it cut off. Many people arriving in England and seeing that everyone is clean shaven start to copy the masses, he said, and this is very bad, i.e. to assimilate yourself and show that you do not wish to keep what is your own. Furthermore he advised me that in all circumstances to keep myself independent; if someone asks you out somewhere you should reply directly "good I shall come, thank you" or "no I shall not come, I do not want to come". There must be no attempt to dissimulate, that from this English point of view is the worst thing you can do, you must be quite independent. Then he gave me some advice about how to conduct myself in daily affairs. On his advice I wrote a letter to Langley telling him I had arrived, that I had a letter from Professor Pavlov and that I will arrive at Cambridge on such-and-such a train.

Arriving at Cambridge I only just stepped out of the carriage when I saw Barcroft beside me; he grasped my suitcase and carried it himself. I wanted to get a porter but he said no, no you are a guest. He carried the case, called the cab man, who immediately took it off somewhere. It appears that in Cambridge there are special rooms set aside in the houses of various landladies for university people. If a landlady has university people she cannot have other lodgers; all such rooms are registered with the university authorities. In twenty minutes we already had a flat for myself with two rooms, the first floor a sitting room, the second floor a bedroom (for I guess that is the English custom) and the ground floor for the landlady; we paid only 50 roubles for the flat and the food.

The English method of working is greatly different from the German. The laboratories in those days were still housed in old buildings and were rather homely and modest; Langley was the head. At that time the great scientist Barcroft was working there; he was already a fully qualified worker with his own assistants. Then there was Keith Lucas, also a qualified scientist, [and] a young man called Archibald Hill who worked there; he [A. V. Hill] had only just written his thesis and was a mathematician who had somehow done two subjects at university, mathematics and physics, but he had no previous connection with biology or medicine. He was a great enthusiast for various sports, particularly running; once whilst he was running the thought occurred to him: how does this muscle machine work? And this led him to the physiology laboratory where he has worked ever since. They all came into work just when they felt like it; only when they were to teach students that they arrived punctually. Lucas arrived when I was sitting there working,

"Good morning sir, I am Lucas; would you like to come out in my motorboat?"

"Thank you."

He sat down. "So tomorrow if it is good weather I will go out and I would like to invite you and your wife to come. If it rains I will come to work in the laboratory. Perhaps you would like to see my experiments?"

"Thank you, I would very much like to see them."

"Well then, goodbye".

In the laboratory each person had his place and conditions were very modest. Gradually I got to know people; a man with a pipe appeared: "I am Hill, what are you doing?" I said I'm operating on a frog; and, "Why are you sterilising the instruments?" To make the operation aseptic. And, "Can frog really have microbes?" I replied, of course they can, microbes can live in the skin. And, "Can they hurt it? I know nothing about bacteriology or medicine, I'm a physicist." He invited me to see his experiments and then he disappeared somewhere. I asked, where is Hill? He is reading at the moment. So it seemed that he read for a week appearing in the laboratory only to smoke his pipe and drink a cup of tea. The next week arrived, where has Hill got to? Hill is at an instrument factory watching the making of his galvanometer. (This of course would lead to work on the heat of muscle contraction.) In other words Hill knew every detail, made specific requests and himself tried out the range of instruments. Then they said Hill has got his galvanometer, after this Hill got to work, where? In the basement, the galvanometer was set up on a special mounting, Hill shut himself up and nobody saw him for a week. Suddenly he finished and came out again and the motorboat was running and all sorts of fun started running up again.

In England it is absolutely necessary to drink tea at 5 o'clock. A small table was set up in the library of the laboratory and a servant brought in a teapot with hot water, made some tea, and set out the cups. Suddenly everyone appeared from whatever they were doing, reading or working, and for the next 30 or 40 minutes the whole laboratory drank tea and exchanged the latest news and then everyone disappeared into their own corner and got back to work. So by the request of Langley it was Barcroft who met me at the platform. Barcroft was already a professor, a solid man 10 or 15 years older than me; he took my things, fixed me up with a rooms and gave me a letter from Langley it said:

"Dear Orbeli,

I would like to talk to you tomorrow morning at 10 o'clock."

I arrived at 10 and Langley said, "I am this very moment just going to do an experiment, would you like to see it?" Thank you. I went to his workplace and he set up the experiment without an assistant; there were no observers and I watched the experiment, and after this he handed me a note in which was written:

"I suggest that you work on such and such a problem, that you find out the effects of sympathetic nerves on X and Y. As a subject for the experiment, you should use the frog. Assistant so and so will give you the frogs, Dr Barcroft will show you your workplace."

They showed me my place and it was a little space between cupboards near the window. The assistant brought the frogs, put them on the table and I started to work. They brought a few things but no instruments and at first I couldn't understand, but I went to a shop and bought my own scissors and forceps – I'd had the chance to see the forceps used by Langley. Four or five days went by, the frogs were somehow strange and I couldn't understand it. They lay flat and no pulses were visible in the blood vessels and I had to discover the influence of sympathetic nerves on the blood vessels. Then on the fifth or sixth day they brought me a long questionnaire: surname, Christian name, age, country of origin, subject of study, influence of nerves of internal organs, animal subject of experimental frog, number required 1000; all this was necessary in order to have the right to operate on frogs.

In England at this time the anti-vivisection league was working actively and in order to gain protection from it a law was brought in allowing certain people to operate on live animals under government supervision. Therefore, there was a particular official who was directed to go from university to university seeing that operations were conducted according to law. It appeared that in these first few days they had given me frogs with the central nervous system destroyed before they were brought to me. A special assistant destroyed the brain of each frog. Only after I got a licence did I start to get live frogs. Once I was present at Langley's experiment; usually each person worked by himself but once Langley asked me to check what he had done and so I asked him to check my results; life went on in this way for several months. One day he arrived with a huge bunch of roses and asked me to give them to Madam Orbeli and he invited us to lunch that day.

Cambridge professors all lived in suburban villas; around the villas there were small gardens with roses; the lunch was very grand. The hostess and the women guests wore hats and the men wore ordinary jackets; I, as is the Russian custom, wore a long frock coat. Each guest was given the choice of two dishes at each course. During the meal wine was not served; only after lunch was finished and the ladies had gone out to look at the garden did they *serve port and coffee to the men, who had stayed sitting around the table. After 10 or 15 minutes the hostess called and said "men, men come here", and then there was a general viewing of the roses. Langley had 40 or 50 different varieties, each labelled. Wearing gloves of thick yellow leather Langley cut off the blooms with scissors and handed them to us. Everything was very elegant and charming, but at work he was dry and business like.*

He was the founder of *The Journal of Physiology* [Michael Foster founded *The Journal of Physiology* and J. N. Langley followed him as proprietor and editor] … and this is where you get into a bit of argumentative history**.**

He himself edited all the articles, wrote to the authors. If something in an article had to be altered, Langley used to tell the author about it, but he would do nothing without his permission. I later heard many good words about him from English physiologists. In spite of the fact he lived in Cambridge and worked alone in his room he seemed to have been the teacher of a good half of all the physiologists in England and therefore a large number of papers were sent to him for comments. He advised the authors how to continue and improve their work; it was immense drudgery; his personal library was taken over to the laboratory so that any workers could borrow what they needed.

If I could just interject here a bit which is not Orbeli**,** Langley really felt that not only did he originate but he owned *The Journal of Physiology*. He was so interfering I believe from what I've heard from various senior physiologists in the past. He was so interfering in authors writing and conclusions that eventually it led to the setting up of the *Quarterly Journal of Experimental Physiology*. When he had died, his widow insisted that she had inherited *The Journal* and I think The Society paid her something to settle the matter, so *The Journal* was the property of The Society. Back to Orbeli:

A very interesting figure in Cambridge was Gaskell. I had heard of him in St Petersburg. He was a powerful figure, tall with a grey tuft of hair and a small grey beard.

Gaskell was a great physiologist too but he had no idea about getting terminologies that suited so his description, his autonomic nervous system was the vegetative nervous system and other strange terminology that would never have lasted. Anyway back to Orbeli:

Physiology in England did not develop for a long time. Although England had Harvey, systematic work did not continue there … Ludwig, Goltz and Hering worked in Germany and France had Claude Bernard, but England was behind as regards physiology. Then at one point Thomas Huxley, the celebrated biologist, was asked how experimental physiology could be organised in England. Huxley indicted that he thought Michael Foster, a young doctor …

I believe he was University College actually, Foster.

… could do much in this direction, so Foster was invited to Cambridge to organise physiological work there. He decided that he himself should not do experimental work but should devote himself to teaching and training up young people. We know of no work of which it could be said Foster did the experiments but he produced a whole series of distinguished physiologists; Schäfer, Gaskell, Barcroft, Sherrington, Balfour – and this group here of great scholars was trained by one man who ended up going into parliament. It was suggested that his place as Professor be taken by Gaskell but because of a sick wife, Gaskell was confined to work at home for 8 or 9 years. From this Langley moved into first place in

the laboratory. Langley did all his work with frogs using only simple eyesight and observation; he used to say, "I believe my own eyes more than any instrument; an instrument may show me something which is not really there, but with my eyes I can see properly." He was furnished only with a microscope, a magnifying glass and dissecting instruments; to a certain extent he was right.

Orbeli writes quite a nice script about Langley a really very nice person. I think he was very much like somebody we had here, Professor [of Surgery, Sir William] McEuan, a very harsh man. In the next wee bit Barcroft [says something on what] Langley was like. Anyway Barcroft told him this following story:

As a last-year student, Langley advised him to study the nervous system of the salivary glands the exchange of gases of the salivary glands on irritation of two nerves; the sympathetic and corda tempani. He had then asked Langley to show him how to dissect them and show me where the corda tempani and the salivary gland duct were. Langley not looking up from his magnifying glass replied, "if you are such a fool as not to be able to find the nerves in the salivary gland then I have nothing more to say to you."

I think that is near enough to Langley as other things.

MR: You mentioned to Barcroft, that's Joseph Barcroft?

JSG: Yes, that's Joseph Barcroft, yes. So I thought a quite good description of what Cambridge was like at the start.

MR: That was very interesting.

JSG: What life was like at the start.

MR: Yes that would be great.

JSG: And the other thing I was going to say something about … because I get correspondence from Sir Henry Dale about it, it was the link between Langley and Elliott (T. R. Elliott, 1877–1961) and that takes us back to the first suggestion that nerves produce their effects by liberating some chemical substance. But Elliott's suggestion that they did so by liberating adrenaline, that suggestion was made explicitly in a pre-circulated communication to The Society in 1904 by Elliott. But when the full paper appeared in 1905, that suggestion is not explicitly made at all and the feeling is Langley suppressed that. It's quite curious. I have read over the years quite a lot of theses which are related to these areas and a number of postgraduate students say that Elliott made this suggestion in 1905, but it's clear they had not read the papers; quite interesting. Anyway, there was certainly some interaction between Langley and Elliott and so I was going to read some of these things from a letter from Sir Henry Dale. By this time he is in a nursing home and he is getting quite close to his ninetieth birthday.

My Dear Gillespie

I do not know to what extent you may be aware of the fact that advancing years and physical disabilities in my own case mainly from accidents have made it necessary for me with my wife to transfer our domicile to this nursing home. Although I need special contrivances and help to get about our present neighbourhood from university has given me the privilege of being present on certain less formal occasions to renew old friendships and *contacts and to make new ones. On these lines Sir Bryan Matthews has been in contact with me to ask me to come to the sherry party at the Physiological Laboratory which is to follow the lecture which you are to deliver to his advanced physiology class and others interested in such matters and in which I gather you are expected to deal with some recent developments to which you and your associates have been contributing on the chemical transmitter theme.*

[The lecture he refers to was] the GL Brown lecture I was giving.

I myself am hoping to be able to respond to this kind invitation and as to meet you among others who are present at this sherry party.

In this connection I have recently received the report of the council of the Royal Society for the year ending (??) and I have had the opportunity of reading your own report to the Royal Society of your year's work as the Henry Head Research Fellow … I suppose incidentally that I am one of the few still living who can look back with [lots] of interest and pleasure to personal acquaintance with, and friendly interest from, Henry Head himself. I think that I can also claim some special interest in your subject through my early friendship and even some direct co-operation with T. R. Elliott. At the time when he published in a brief note in the Proceedings of the Physiological Society *what I still regard as the first definitive and specific proposal of a chemical transmitter process for the effects of nerve impulses, although I suspect that, for various reasons, it is now for many years almost been forgotten. I was in these early days for a time one of Elliott's few convinced backers. I see that you and your colleagues are probing for good reason more deeply into the nature of the altered mechanism of the transmitter process connected with the true sympathetic or more strictly adrenergic nerves and are dealing almost exclusively with noradrenaline. I suspect you will agree that the special interest of noradrenaline …*

Later in the letter he is going to take me to task and hopes I am not going to be pursuing this concept of noradrenergic which is quite unnecessary.

I suspect you agree that the special interest of noradrenaline rather than adrenaline in that connection applies particularly to the mammals and perhaps to those which have become regular subjects of physiological experiments. I am just thinking of the probability that the chemical transmission of the sympathetic effect first directly demonstrated by my friend Loewi in the frog's heart is likely to be due to adrenaline itself. In any case I have to remember against myself my own first detailed comparison of adrenaline and noradrenaline with respect to the proportionate representation in the activities of augmentory and inhibitory sympathetic effects. I was actually rather staggered to find in this respect the action of noradrenaline was even more closely sympathomimetic than that of adrenaline itself. Noradrenaline of course was at that time only a new sympathetic curiosity made by Stolz of the Hoechst firm. Nobody then had any reason to suspect that it would ultimately be found to be a constituent of the secretion from the suprarenal medulla or to be in any sense a natural physiological substance; and in my paper, in which this finding was discussed, I'm afraid I made it only too clear that it had, for a time, shaken my own conviction in Elliott's brilliant hypothesis.

It then goes on to say because he is in a nursing home will I send him some re-prints, so I sent him some re-prints – so that is 10th November 1967 – and so I sent him re-prints.

This is a handwritten one and he's 92 and he is writing well, anyway going on from there:

My Dear Gillespie …

That was when in the days we were writing there was a greater intimacy. I always found a great difficulty in writing "Dear Hodgkin".

MR: You never used first names in those days?

JSG: No if it was somebody you knew it was "Dear Hodgkin".

My Dear Gillespie

I was glad and grateful to have your good letter of November 16th of the enclosed very interesting and useful re-prints of your publications. You have been making valuable use of the possibility of obtaining fluorescent photo-micrographic images of noradrenaline deposits near the endings of sympathetic fibres and when applied in higher concentrations on the "receptors" of chemosensitive plain muscle fibres. It is a pity that similar but distinctive visible indications cannot be obtained for adrenaline. I can't however agree with your suggestion that we should complicate the nomenclature by introducing such a distinctive derivative term as 'noradrenergic' into general use. If you have access to a series of Journal of Physiology *…*

I'm creasing up here! "*If I've got access to them*!"

… you will find in volume 83 pages 10–11 1933 a short note in which I suggested the term 'ergic' and then I think for still good reasons, defined my object as to coin words which will briefly indicate action by two kinds of chemical transmitters due in the one case to some substance like adrenaline, *etc. I deliberately left the definition to that extent vague so as to make the work applicable to transmission also by noradrenaline in the event of the evidence being obtained for its presence.*

MR: At what point did the Americans ... because they taught more [using] "epinephrine"; did that all happen at the same time?

JSG: No that appeared earlier and Dale has got an account of that and it's all tied up with an attempt … now which was the company? … to patent [the name] "adrenaline" and that attempt to patent "adrenaline" led to them moving to epinephrine and it was a Japanese; something sneaky there I'll need to think about. Anyway …

… being obtained with its presence as such in the body and for its function as transmitter which did not happen till after *1933. If measurements of the ratio between augmenter and inhibitory action without artificial stimulation of a particular postganglionic sympathetic nerve were to indicate a mixture of adrenaline and noradrenaline transmission there it would be nothing as yet to indicate whether the nerves contain adrenergic or noradrenergic fibres or whether, which I shall at present regard as equally probable, the fibres of that particular nerve in its particular animal species all used a mixed adrenaline and noradrenaline transmitter. Already the Americans are confusing the poor British journalists by writing about norepinephrine and giving them the idea that this is a great new discovery. I shuddered at the possibility, by no means remote, of "norepinephric" transmission; I hope you won't do anything to help its arrival.*

You evidently agreed with me in lamenting the fact that Elliott's priority in first definitely suggesting these specific chemical transmissions has been so largely forgotten. I'm afraid that that old rascal Otto Loewi played a part in bringing that about in his description of the manner, etc. of his own very important experiments.

… and that's the Vagusstoff …

He mentioned a remark which he himself had made to Walter Fletcher when Fletcher was visiting Meyer's department at Marburg [Germany] in 1903. They went for a walk together and Loewi suddenly remarked to Fletcher, "Why shouldn't the vagus impulse inhibit the heart by secreting muscarine from its fibre endings?" Or words to that effect. Loewi had completely forgotten the remark as he himself has admitted, but Fletcher [was] reminded of it when Loewi's first epoch-making experiment on the frog's heart was published. But Loewi had by then also forgotten rather conveniently that, shortly before, Fletcher had visited to Marburg. Loewi, who had been for a month or more in Starling's department in London where I was then working, took a week or more off for a visit to Langley's department in Cambridge. On his return to London he spoke to me with special enthusiasm of the impression made on him by the brilliance of young Elliott but Loewi never mentioned in connection with his own demonstration [of] such a mechanism. Vagusstoff and sympathetic Vagusstoff [and] Elliott['s] note [to the] Phys Soc in 1904. Nor for that matter did he find it convenient to mention H. K. Anderson's description of the action of physostigmine in reinforcing the effects of impulses in the short ciliary nerve fibres in the pupil, losing its effect when the fibres degenerated and recovering it as soon as they regenerated; this was published by Anderson in Journal of Physiology *[in the] early 1900s. Before Elliott and I began, I myself scolded Elliott for still writing about the Vagusstoff in 1921 when I myself had seven years earlier just before the World War began pointed out if there were direct evidence for such a chemical transmission as Elliott had proposed, acetyl choline would have ideal properties for a parasympathetic transmitter. Loewi actually said to me of course I know it must be hard to tell colleagues but I am afraid to say so, only two years ago I published a mistaken conclusion about another research matter and had to withdraw it and then if I make another mistake they will all be delighted to write me off!*

I must tell you some other time about the several reasons for Elliott's early ending of physiological research in which he had shown such early brilliance. There were too many factors and some too personal for record in a letter like this. I hope I shall be able to meet you at Thursday night's meeting.

I was looking forward to learning these very personal facts, but his wife died and he couldn't come, so that was kind of sad but I believe that – for a variety of reasons – Langley was a most particular experimenter, very exact and everything done thoroughly and you felt Elliott was too quick to speculate. Of course Elliott gave up physiology altogether and became gynaecologist although Henry Dale kept in touch with him for many years.

TCM: They were all pacifists; I think Elliott went to the First World War if my memory serves me right. Elliott published with Langley and I think Elliott went to the First World War; he is the only one …

JSG: Was he a dashing Major wasn't he?

TCM: Was yes.

JSG: And he did a lot of work on blood transfusion which was a problem but never really got the hang of it but was a thing they very much needed in the First World War.

MR: Did you have a close connection with Henry Dale?

JSG: Well let's see, yes. I mean a close connection in so far as the gap in ages and distinction was so high but I met him a lot at meetings and so on.

MR: But Feldberg you were close to?

JSG: Yes Feldberg would have been closer to me, but Dale I felt was a very revered figure, he really was.

TCM: But your link with G. L. Brown was closest?

JSG: Oh yes.

MR: Was Brian Davies around when you were?

JSG: Brian Davies took over after me; he came after me.

MR: Oh because he was a colleague of mine at Barts

JSG: Of course he was.

MR: Still in touch with him now.

JSG: Yes. It's a continuation of this business to some extent I had given a talk – I can't remember what the occasion was – in Gothenburg, about historical aspects of physiology of transmission and particularly I took up Langley and Elliott, trying to bring out you know that Elliott made that very prescient suggestion of chemical transmission and he was right and Langley was wrong. But later on when it came to the concept of receptors, which is much more solid, Langley was right, he was absolutely right, the concept that there were these special substances on which chemical acting in the cells produced their effects. Anyway after I had given that talk I got a wee letter from Hugh Blaschko [Hermann Karl Felix (Hugh) Blaschko, 1900–1993]; Hugh Blaschko's dead I think. I think towards the end of his life he went back and called himself "Hermann" I'm sure he did. Anyway:

Dear John,

I tried to see you after your nice paper at the Gothenburg symposium but I never saw you again. From Gothenburg we went to the Trendelenburg meeting in France; I then came home on Tuesday and find we have bits of an article that I had just written for comprehensive biochemistry over a year ago. I'm going to photograph two pages that contain the link I mentioned at Gothenburg.

Its says … he is not an awfully good writer:

It is odd that this remark has been completely overlooked in general since I have turned [into] a "historian", I have made the experience that the …

Can you read these two words there?

TCM: I can't make that out, sorry.

… stories for example Bacq, Dale, etc. are never quite complete, they always omit something; the only way is to treat history just as you would treat phrenology: trust no-one, always go back to the original sources. In the meantime I am basking in the reflected glory and rejoice in David Smith's election to succeed Bill Paton.

He also sent me a copy of these wee bits and some of them are quite interesting.

This leaves little doubt that Gaskell had the transmitter concept in mind when he wrote these lines [...]. He must have been aware of Elliott's earlier suggestion. Elliott did not refer to it again when he published his full paper in 1905. One can only surmise what the reasons were for this omission. Probably the idea had been met with some criticism when he read his paper to the Phys Soc in 1904. This is similar to Dale's interpretation in the biographic memoir he wrote on T. R. Elliott. He refers to Langley's unwillingness to accept speculations. Elliott made only one further explicit reference to the earlier vote and this was in his Sydney Ringer lecture of 1914. There he writes:

"The theory which I had at first held to explain these facts was that the nervous stimulus consists in a liberation of adrenaline itself from the ending of the nerve on the muscle. We have seen how the ganglion cell and the adrenal cell are both derived from what is almost a common cell with power to transmit a nerve impulse or to excrete adrenalin. It is very conceivable that as the nervous cell developed its peculiar outgrowths for the purpose transmitting and localising the nerve impulse it might lose its power of producing adrenalin and come to depend altogether on what could be picked up from the circulating blood and stored in its nerve endings."

Now, that's the first time I've ever seen such an early reference to neuronal uptake.

Apart from part of the last sentence, we know today that the adrenergic neuron has the ability to produce catecholamines. This statement substantially conveys the picture that we consider as valid today. The original idea of Elliott was criticised also in the well know paper of Barger and Dale which introduced the term "sympathomimetics". Over 40 years later when the paper was re-printed Dale adds this comment:

"Doubtless I ought to have seen that noradrenaline might be the main transmitter but Elliott's theory might be right in principle and faulty only in this detail."

I was very interested to see that in Elliott's lecture of 1914 the idea of amine storage is already discussed. This is of relevance not only in view of much later work by J. H. Burn and last discussed by him fairly recently, but also with regards to another piece of work carried out in Cambridge in the first decade of this century and is of historical interest for the history of the transmitter concept. W. E. Dixon, Professor of Pharmacology at Cambridge, was engaged in a study of the action of the vagus nerve on the heart. Dixon and Hamill discussed the possibility that the action of the vagus on the effector organ might be mediated through the release of some muscarine from nerve endings upon stimulation of the nerve. Like Elliott's earlier suggestion, this idea did not find favour with Barger and Dale. In particular they criticised in the additional proposal Dixon and Hamill thought that, if their idea was true, there might be some substance that exerted a pharmacological action, not by virtue of any intrinsic muscarin-like properties, but indirectly by displacing some of the "natural transmitter" from its storage site. Barger and Dale dismissed this idea; they found it difficult to draw the dividing line between what we would today call "directly acting" and "indirectly *acting" substances. It took almost half a century until support for such an idea came from Burn and Rang.*

There is one additional group of early papers in which a biochemical approach was taken and in which humoral transmission was foreseen. This work I was not aware of until Anika Dalstrohm [...] and David Smith both referred to it, about 10 years ago. It is the work of F. H. Scott and his approach was a cytochemical one. He made a study of the material usually called the Nissl body present in nerve cells. He found [them] not only in nerve cells, but also in secretory cells, such as an exocrine glands of the pyloric and the secretory cells of the fundus of the stomach. He convinced himself that the chemical properties of this material were those of a nucleoprotein and he postulated a close analogy between the functions of a glandular cell and the nerve cell and then there was a quote from his paper.

"It seems simpler to suppose that the nerve cell secretes a substance the passage of which from the nerve ending is necessary to stimulation."

It seems remarkable that Scott's prophetic words were overlooked for so long.

I think I will leave this next bit out … but in these things both uptake and direct and indirect actions of sympathomimetics were also seen as well as chemical transmissions, really quite a long time ago […]

MR: Maybe you should finish off with a bit of free speaking – you know?

DJM: You have not said much about your time here and the development of the Pharmacology Department from Physiology as was. You did start off by talking about the bits falling off physiology and becoming full blown disciplines in themselves, do you want to say a bit about this?

JSG: Well of course pharmacology existed … no, pharmacology did not fall off physiology. Pharmacology fell off Materia Medica. That is the study of drugs was always part of the clinical subject of materia medica and then over the years scientists not medicals were employed. We had Jimmy Graham here at one time. Before that I cannot remember the woman's name … Mary Lockyer? … Lockhart?

MR: Lucy Lockhart?

JSG: No

TCM: No, she went to Australia.

JSG: Yes I can't quite remember her name but she was the first to establish an animal house if I remember then. John Lewis was the man who built up within the materia medica, the quite substantial experimental pharmacology in which Tom, here, was a member, David Pollock, Frances [Boyle], Willie Wilson; they were all people who were later in the Pharmacological Department but who were with John Lewis in Materia Medica.

There had always been a feeling that pharmacology was developing as an independent science and so at one point there was a suggestion that I might go and move as the first professor of Pharmacology. We did that and in a discussion with the professor of Materia Medica we agreed that the third floor would be allocated to the new Department of Pharmacology. We set it up and I must say it was a great time because we had an enormous enthusiasm from everybody in the Department. We had to make up classes for the medical students, not just lecture classes but practical classes for medical students and for junior and senior honours science students and so on and for the dental class, and I think they were quite good. We then developed an honours class that became quite big; many of the people now have chairs and are heads of departments.

Originally we taught in collaboration with Physiology so we only had one combined physiology–pharmacology exam but eventually we had as external examiner Jimmy Black and Jimmy was convinced we should have the departments separate, and we brought that to our Principal and eventually we separated off the two subjects, so that is basically the background to that.

DJM: So links remained strong with Medicine because of the key place in the medical curriculum. But what about links to, say, Chemistry which here has always been large and strong?

JSG: Yes, I would not have said we had strong links with chemistry.

TCM They were diminishing links in that we had Mike Martin-Smith from Chemistry to set up a synthetic chemistry lab, probably before you came [John]. That laboratory had one or two students, but then when Martin-Smith was appointed at Strathclyde, their position as chemists became more and more anomalous and then in fact eventually the chemical laboratory disappeared. John came in 1968?

JSG: That's right.

TCM: Then in fact it was a Pharmacology department for the first time; it was a division before that and then John came – he was the first professor of Pharmacology; these were exciting days.

He hasn't really mentioned his great ability to get people to work with him. John had the ability to make Pharmacology [...] a very happy place. It was one where you enjoyed the experience, you were never allowed to forget your responsibilities and you were expected to contribute to the societies which as professional bodies were in fact representing your profession, so we were all involved in the affairs of the Pharmacological Society and of The Physiological Society. I think he achieved that because he was particularly interested in the people with whom he worked. I'm sure, speaking personally, he took a great interest in all that we did and all that could contribute towards The Society and in the profession. For that we are all entirely grateful and that is why we became such a very active and interesting department.

MR: How do you respond?

JSG: Oh I couldn't respond to that!

MR: Oh please!

JSG: Not at all. All I remember is that these were great days and I enjoyed them tremendously. Eventually I got side-tracked into administrative work in the University by becoming a Vice Principal and so on, which is not a job I was all that interested in at all. I mean, I did my best, but it's not as interesting as laboratory work and the contact with students and staff.

At one point I was going to read you … One of the things in the early stages around the '50s there was a great deal of exchange between the scientists; jokes were played, games were played. G. L. Brown was a great ballad writer; you probably knew that?

MR: No I didn't.

JSG: Oh he was a great ballad writer and so was Bill Paton. They wrote one in particular which was well known at the time about … oh God what's his name? [Haldane] "His wife is standing on a doggies' tail …" but the other things were the kind of letters people wrote now you probably all know this ones from Harold Lewis, have you seen it?

MR: Was this the one about the sphygmo [manometer] …?

JSG: Yes that's it.

MR: Yes well they often give that one.

JSG: Yes well I'm not going to go into that, but there were all sorts of others I had here, the [...] society.

DJM: So was that really because they had more time for these things or were they just interested in these things?

JSG: They had more time, we all had more time. You know you had to read up and write your lectures and we lectured more I think than people lecture now. We all did the first thing in the teaching labs which is a pleasure but we never in the early days had any contact "up the Hill" [the administration of Glasgow University] at all.

MR: Money wasn't an issue then was it?

JSG: No, money wasn't a great issue because in the great days of the kymograph once you had a kymograph that was it for life and your recorders and so on and most of the experiments could be done.

MR: And the software didn't need upgrading did it!

JSG: None of that sort of thing and I mean the university was run by three people; we had a Principal, Hetherington, we had a Secretary of the Court, Robert Hutchinson, and a Finance Officer, McKean, and these three people would run the University. I mean you had typists and clerks and so on but in terms of the administrative people I mean it seems to me now, and I could see it before I finished, that more and more academic people were sucked into administration. I mean it wasn't just that we had more and more administrators; administrators were coming mainly to be academics who were sucked into it.

MR: The student numbers weren't much different then?

JSG: Oh yes.

MR: They were?

JSG: Oh yes. We had great discussion in Senate as to whether we could go up beyond to 11,000 students.

MR: For the university the numbers must have stayed the same for the medical students.

JSG: Well the medical students' status stayed the same. I'm not sure what it is now, but 14[000] sounded possible. Everything has gone up. I don't know what it is today.

DJM: Well over 20,000 now.

JSG: Twenty thousand, oh that's about right. So I think people had more time …

MR: It was a post-war era wasn't it; everybody was more relaxed.

JSG: There was the great post-Robbins era you know because that idea that everyone who has the capacity to benefit from a university education should be financed and supported to go there. That led to a big increase in staff because money was made available for these students and the numbers of staff were greatly increased. I guess it was at that period, towards the end of that period that they decided to establish a separate Department of Pharmacology because this was a possibility as the funds hadn't been available before.

TCM: But I was always impressed by […] the interest that these people had in personal matters. I can remember my own case was when I last met G. L. Brown was when I was flying home from Sydney and he said, "Don't fly Pan Am". And I was booked to fly to Pan Am! [R. C.] Garry had told me that I had to remember that the Prime Minister of Australia was not Robert Menzies but Robert Garry Minges […].

DJM: Any particular research students John? It might be invidious to name one …

JSG: Let me have a think … In some ways you remember the ones who didn't make an impact on you and who did so well later because that remains you know a puzzle, you wonder about that. The two people there was Graham Henderson; he was a very quiet person as far I was concerned he was very quiet boy as a student and I would have not realised he was going to do as well as he has done. There was another man […] John McGuigan. He's done outstandingly well, but he didn't impress me as a student so much. Some of the girls I remember impressed me no end. This was back in Physiology with Frances Boyle as an Honours student and another girl, oh what's her name? She became a professor, she was very good, what's her name?

TCM: Not Marjorie Allison?

JSG: No it wasn't Marjorie Allison at least I don't think it was. Anyway this girl did her research project and I remember her analysing it by probit analysis … I had absolutely no idea what the probit analysis was!

DJM: OK, well the time has shot past but – if you are happy to stop here, John – thank you very much indeed.

An obituary of John Gillespie by Ian McGrath was published in *Physiology News* (issue 78, p. 56; http://bit.ly/1mAv7fL). An obituary by Tom Muir and Billy Martin was published in the Glasgow Herald (10 December 2009; http://bit.ly/1fGb25U).

Left, David Miller and Tom Muir with John Gillespie, photographed by Martin Rosenberg;
right, W. Martin, J. S. Gillespie, T. C. Muir and J. C. ('Ian') McGrath, photographed by David Miller.

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