

## Peter Harper



### **Personal Details**

Name	Peter Harper
Dates	Born 28/04/1939
Place of Birth	UK (Barnstaple)
Main work places	Liverpool, Baltimore, Cardiff
Principal field of work	Clinical genetics, Neurogenetics
Short biography	See below

### **Interview**

Recorded interview made	Yes
Interviewer	Angus Clarke
Date of Interview	03/09/2004
Edited transcript available	See below

### **Personal Scientific Records**

Significant Record sets exists	Yes
Records catalogued	In progress
Permanent place of archive	Cardiff
Summary of archive	

## **Biography**

Peter Harper was born in Devon, England and was educated in biology and medicine at Oxford University and St Thomas's Hospital London, qualifying in 1964. After a series of medical posts he worked in Liverpool with Cyril Clarke in genetics and medicine, followed by a two year fellowship with Victor McKusick in Baltimore. Returning to Britain in 1971, he established a medical genetics unit in Cardiff with a particular emphasis on inherited neurological disorders, his group being among the first to apply molecular techniques to inherited disorders. A member of the Human Genetics Commission and Nuffield Council on Bioethics, he also developed a major interest in documenting the history of the field, founding the Genetics and Medicine Historical Network in 2003, and in 2004 was appointed University Research Professor in Human Genetics at Cardiff University (now Emeritus), to develop this field.

## **INTERVIEW WITH PROFESSOR PETER HARPER, 3rd SEPTEMBER 2004**

Interviewer Professor Angus Clarke.

AC. I suppose the place to start is the beginning, if you want to say a bit, Peter, about your family and your childhood

PSH. I suppose the main thing to say is that I think I was very fortunate in many ways. Fortunate perhaps time-wise, because although I was born just 6 months before the last war broke out, it didn't seriously disrupt my childhood, and although my father as a doctor was doing all kinds of very hectic things, nobody in the immediate family was directly involved or killed in the war; so that compared with many people a bit older that wasn't such a problem, and fortunate also because I came from a family which I think I had a lot of advantages from. A very medical family I have to say, my father was a physician and a very thoughtful person, with a major interest in evolution and so as I grew older we could actually have a lot of shared interests on natural history and evolution and then a bit on genetics later on. My mother wasn't medical but she was also a very scholarly person. I think you know she died a year or so ago at the age of one hundred, and she was actually a French scholar, and just after the first world war spent two years in Paris and did a doctorate there; and she wasn't medical at all, but actually she came from a medical family, in Shropshire, whereas my father and his family were all from Barnstaple in Devon, so I grew up in a small town, which is actually a rather nice kind of place to grow up in, particularly those days.

AC. Sort of like Jane did in Brecon

PSH. It was very similar, very similar, perhaps even more so, because in those days, by which I mean I suppose the late 40s early 50s, small towns I think had a lot more character. There were no chain stores, there were lots of small shops and craftsmen and you could wander around and for a kid growing up there were all kinds of interesting things and then, it was a small enough town, you could get on your bicycle and go out places. There wasn't much traffic. You could just wander around and it was very enjoyable.

AC. At what point did you see your way heading into science and medicine?

PSH. It's quite difficult to pinpoint, because I think I kind of absorbed medicine all along although I don't think my father ever, he certainly never pushed me that way, but it was part of the system, and I think in those days people lived over the shop, and my father was first in general practice and then when the Health Service came in he became a consultant, but I was always used to patients being around and consultations in the house, you know, father being called out at all kinds of inconvenient times. So that was there, and I think the science side was partly because I was always very, very keen on anything to do with natural history and I think it started, I think I was definitely one of those people who had a sort of collecting mania, and it started with more or less with anything you could think of but sort of, focused down onto things like butterflies and then gradually shifted away from collecting. . .

AC. Not birds eggs!

PSH. Never birds eggs, no actually. In fact I was never terribly knowledgeable about birds even. It was insects at the beginning, but things in general and then I was very lucky. I had a really quite inspiring zoology teacher, who was a very unorthodox fellow and probably wouldn't be allowed anywhere near teaching now. In fact I'm sure he wouldn't, but he was one of these people who was just inspiring, so I did zoology for A level, or whatever it was then, and was lucky enough actually then to get a scholarship to Oxford and then had to choose, did I do zoology or biology at Oxford or did I go for medicine. That was difficult and I think my father might have steered me a bit then, because he said well, if you are not quite sure, if you get a medical degree at least you will have something to do and if you change your mind part way through, well you can do that. One way or another it will stand you in good stead. I think he was right and . . .

AC. Change in the other direction is harder.

PSH. Yes, it would have been much harder, but the only slight problem with that was, as you know yourself, that the medical Oxford degree was coupled with physiology and I spent my whole time essentially in the zoology department. That was fine, because Oxford then was the sort of place where they didn't bother if you went to all the wrong courses, but it didn't actually help your exams very much at the end of the time, and I remember my tutor saying you've got two alternatives, you can either spend all your time studying zoology and you'll get a reasonable degree but not a very good one, or you can spend all your time doing the things which the exams are going to be on and you will almost certainly get a first; and I chose going to all the zoology things and as a result didn't get a first, but I didn't do too badly. So that sort of launched me into the area because the Oxford department of zoology then was fantastic. It was essentially evolutionary.

AC. J Z Young?

PSH. Not J Z Young, no. It was Alistair Hardy, then people like Niko Tinbergen in animal behaviour, Charles Elton in ecology, Bernard Kettlewell and E B Ford who were on insects and genetics and Arthur Cain in taxonomy; a fantastic lot of people and so I went to all their lectures and never had any exams, and then in the summer I spent several summers doing field work on population insect genetics, mainly up in the northern isles and so I really got into what was more population genetics than anything else and carried that along as an interest, and then I went to London to do my clinical training; so that's how the genetics started.

AC. And Oxford didn't have a clinical course then did it?

PSH. It did, but it was small and a good three quarters of the people had to go to London, which I was actually quite keen to do, because although I loved the years at Oxford I had the feeling it was time to move on after four years which I had spent there.

AC. And there wasn't yet a strong clinical medical interest in genetics in Oxford?

PSH. There was none.

AC. No.

PSH. Actually I'm probably wrong, because there was Stevenson's Unit but it was very disconnected and basically no, there was nothing clinical.

AC. Nothing that catered for medical students?

PSH. No. The only person who was around, strangely, at the time but I never knew it, was Derek Roberts, who was first with LeGros Clark in anatomy and LeGros was another person who influenced me a lot, and then he, Derek Roberts, for a short time was with Stevenson, but no, there was no medical genetics whatever.

AC. And in terms of the different London clinical schools do you think there was any benefit with hindsight genetically in going to St Thomas's?

PSH. None. Most definitely none. There was nothing relevant. If I had known I probably should have gone to Guy's where Paul Polani was. But I didn't and nor did I actually have any contact with the Galton.

AC. Or University College?

PSH. Exactly. I didn't and that was perhaps a pity. It might have altered things if I had but, as it turned out, although the training at St Thomas's was virtually non-existent in terms of anything structured, that was no problem because again, a bit like Oxford, they didn't bother about what you did and it gave one plenty of time to learn from patients, because in those days, Lambeth had a big population, very poor and there were lots of patients and I absolutely loved that, and so that, really during those years, that confirmed that I definitely wanted to do medicine. And so the question rather became, how can I combine the two, rather than am I going to do one or the other.

AC. When did you systematically decide, I will combine the two as opposed to I will pursue a medical career and have an interest on the side in other genetics, evolution and so on.

PSH. I think it was before I qualified, because I remember even doing a busy surgical job taking a PTC tasting kit with me to try and see about patients with appendicitis, which, I mean it didn't go anywhere, but it showed I was still thinking about that, and after my pre-registration year, I definitely was serious then and I'd asked people, asked people back at Oxford too, and they were unanimous that the person was Cyril Clarke in Liverpool, that he was the only person where you could combine the practice of medicine with genetics, and of course the people were right, so after that pre-registration year I went up

AC. Your first SHO post?

PSH. Well no, at the end of that pre-reg year, I went up to Liverpool, saw Cyril Clarke, who was very courteous and listened to me and when I said I would like to go into medical genetics, he immediately said, go away and get your membership and come back when you've got it. Which I was a bit crestfallen about, but of course he was absolutely right. So that's what I did, so I put on the side genetics and did SHO jobs for the next 2 to 3 years, first in paediatrics, and I did that up in Derby Children's Hospital; then I did neurology and neurosurgery at Southampton, which was long before it had a medical school. Then I did some more general medicine and took my membership and got it, and then went back to Liverpool to Cyril Clarke to say, look I've done this, and so he said well apply for a registrar, medical registrar job. Because there were no training posts in medical genetics.

So I applied for the next one and this was quite strange actually, because Liverpool as a whole, quite separate from Cyril Clarke who was very different, the Liverpool Medical School was a very traditional, pretty backward medical school and it was unheard of for anybody to apply for a registrar job who hadn't been trained there. So I went up and had an interview and they looked at me thinking, you know, I must be crazy. You are from outside. Why are you applying here? And they gave the job to somebody else. And then when the next one came up I applied again, so by this stage they realised I must be serious. Anyway I got that and of course it was an ordinary very busy registrar job, but then all the people working in genetics were also practicing medicine. Cyril Clarke was a physician, Richard McConnell was a physician, David Weatherall, he was a physician and a bit of a haematologist. So all these people there were doing great things in genetics along with their current day job and that's what I did. So I mean, I did my busy medical job and attached myself immediately to Cyril Clarke, who got me involved with what gave me just about my first publication, on their big families with inherited oesophageal cancer that had been found a few years before, and so that was my first sort of clinical genetics job, and actually at the same time I had carried on the insect genetics because Phillip Sheppard, who had moved from Oxford to the Liverpool Genetics Department and was working on a lot of things with Cyril Clarke, and I did a project, a couple actually, one out on the Ainsdale dunes and another in the city working on melanic moths.

AC. It was that era wasn't it?

PSH. It was. That was actually my first publication, in Heredity, on that and then my next one was on inherited oesophageal cancer, and that was Liverpool.

AC. How much of the interest going on at Liverpool at the time was related to haemoglobin disorders, perhaps in tropical medicine, was there a strong interest there? Did it connect?

PSH. Didn't quite. It didn't quite. There was a bit. There was a guy called Herbert Gillies who, I think he was a senior lecturer in tropical medicine, who also had some interest in the genetic aspects, and then David Weatherall was starting to develop that, but it didn't tie in . . .

AC. That wasn't the routine for Liverpool

PSH. Not really. The big excitement of course at Liverpool then, it was at the peak of the rhesus work and that had just been published and large scale trials of rhesus immunisation were being organised and the Nuffield Building for medical genetics had just been opened, and so it was very stimulating; so they had good facilities, good labs. Everything was happening. It was a very good time to be there and it meant that people like myself could slot in and the rest of the Liverpool medical scene accepted that, because Cyril was by that stage very well-known. Everybody I think there thought he was crazy, but because of the rhesus work and things, he was highly respected and so the fact that I was working with him gave me a bit of a passport and explained to people really why I was coming from outside.

AC. And had they set up in either medicine or genetics, had they set up a wide range of protein based genetic markers for family studies or not really at that stage?

PSH. Not really. They had lots of blood groups, but I think for the other markers they were tied in very closely with the Galton and with people like Jim Renwick and Sylvia Lawler and with Penrose at the Galton, and so I think for the linkage work they pretty well relied on them.

AC. And how long were you in Liverpool as an SHO?

PSH. I was two years and the one thing that wasn't in Liverpool, there was no clinical genetics, because the bizarre thing was that, although Cyril and the other people were all excellent clinicians, they didn't have the concept of medical genetics as a service

AC. Talking to families?

PSH. There was almost none. There was the occasional family but there was no system of genetic counselling clinics

AC. Only at GOS wasn't it, that that had begun?

PSH. And Paul Polani. But, so it was very clinical, but Cyril's concept of genetics was something that should be an integral part of medicine, and the extraordinary thing was that he was absolutely right, but 30 years too soon, and he was quite opposed to medical genetics as a specialty, because he said that would stop it becoming part of everything else, and there he was wrong. But the good thing was he that had a very close link with Victor McKusick, so lots of people from Liverpool wanting to do more research, or go into more typical medical genetics, would go off to Baltimore and some would go into genetics and some would come back into general medicine, but people like, for instance, David Weatherall and David Price-Evans and quite a few before me had gone there, and when it was clear to Cyril and myself I think that I wasn't going to learn any more *medical* genetics there, he fixed for me to go out to Baltimore to Victor McKusick and that's what I did.

AC. You were there two years?

PSH. Two years. I went out there, I was in Liverpool '67 to '69 and then Baltimore. I went in the Autumn of '69 till Autumn '71, so it was two years and it's like all these things, one would have liked to have a bit more. Things are just getting going during your second year, but on the other hand having a deadline is always a powerful incentive, and I remember collecting my thesis from the binders the day before the plane went back, and by then of course . .

AC. That was on DM. [myotonic dystrophy]

PSH. It was yes, but then by that stage of course, Elaine and I had got married in Liverpool and so we went out with one small child and came back with two, and so there were all those aspects to think of, and the strange thing was that Liverpool, I think I said already, was very inflexible in some ways and it only had one lectureship in medicine, the whole medical school, and that one lectureship came vacant after I had been there about 8 months in America, so I got a letter saying this was coming up and they would like me to apply. They may not have put it as strongly as that but they were quite encouraging, so I wrote back saying I was just getting stuck into things and I really felt there would be no sense in coming back from America and interrupt my training just as I was getting on. Was there any chance of things being deferred? and they wrote back quite simply saying no, if I was interested I would have to come back and if I wasn't interested that was that. And so that was that, and so I didn't go back to Liverpool; and then of course when I was in America that was myotonic dystrophy.

AC. What was the balance between genetic clinics and the broad exposure to things and the focusing on your project on myotonic?

PSH. Again, I struck Johns Hopkins and Victor McKusick's set up at a superb time. There was a mass of research fellows and some of them were clinical and some of them were lab and everybody was mixed in, and it was just like our set up. People were shoe-horned in. If you were lucky you'd have a whole desk and everyone was absolutely crammed, and some people were good clinically and others less good. Quite a lot of people from different countries. A number of quite senior people who had gone into a specialty and wanted to learn about the genetics of it. So there was a real mixture, probably about 15 or so fellows doing all kinds of things, particularly the early gene mapping, and then there was a clinic day once a week where everybody had to be there, drop everything else and see patients, and in between you could get on with your own work and they had a series of genetics nurses who helped and so you got a good range of clinical problems, because there were lots of people came down from the Amish community and there were a lot of bone dysplasias, so you saw this fantastic range, quite, quite unbelievable range of different things, whatever you were doing; and Victor was always very keen on having the British clinical research fellows, because I think we were all pretty well trained. We all had a very wide training whereas some of the American ones had specialised very early into neonates or something and really weren't up to much with wider diseases. So during the two years I must have seen just about everything in the book really, and I got into myotonic dystrophy, not so much by accident, but when I started, Victor suggested why not do something on osteogenesis imperfecta and look at the recessive subset? And after . . .

AC. Just as well

PSH. That's right! After a month or two I ploughed through about 500 files and found about 3 families which might have been recessive, and probably they were all mosaics or something anyway, and Victor said, no this isn't going anywhere, and at the same time that the project had started on myotonic dystrophy a girl called Marian Rivas, who sadly died quite recently, pretty young, and she was a PhD, not medical, very well trained in linkage and she had got going on this, but of course found that she couldn't get anywhere because she had to score all the patients and family members as affected or unaffected and that was really a tough job for a clinician, let alone a non clinician; so we teamed up, the two of us, because it meant then visiting families, essentially the whole of eastern, north east United States as far north as New York and west as Chicago and Indiana, Virginia, the Appalachians and so we had all this family work to do, and bringing back samples for linkage, and also I took a portable slit-lamp to score all these people, just the same as we had here, remember the one that Susan Huson lost?

AC. Yes.

PSH. Carried it all round in the car, and that was a pretty amazing experience actually, in sociological as well as genetic, because it showed you the poverty of rural America, of these families living in terrible situations really, but extraordinarily welcoming and I think it was just quite a unique experience.

AC. How did they get access to Johns Hopkins medical care if they were so remote?

PSH. Well a lot of them weren't under Hopkins, they had been seen at other places but were on the records of various other set ups. The ones who were in the Baltimore striking distance, there was a system, they had a medicare system which actually worked very well. You had to fill in some forms and, provided you did that and particularly provided something was being done as part of the research, that covered everything to a very high standard, so there was some advantage and incentive to these folk to take part, but for those who weren't connected they didn't really have any medical care at all. It was actually pretty dire and I think things have only got worse probably. So I mean, I spent most of those two years driving around parts of north America. Quite a few times Elaine was able to come too, so we went to places that you would never have gone to otherwise, and at the end of it there were a number of vicissitudes which I won't go into, because Victor was not good at running a department. I mean, to be specific, the person who ran the blood group and the linkage lab was not on speaking terms with Jim Renwick, who did all the computer analysis and came over from time to time, and I found myself in the situation where each of them said they wouldn't do anything if I had anything to do with the other, which was, you know, pretty impossible for someone in my position. Victor was no good at sorting that out, but by some miracle I got my thesis completed and a couple of papers written and then there was the question of, you know, you needed a job back at home.

AC. One of your papers was the apo E linkage.

PSH. It was before apo E, it was secretor and Lutheran. It's very strange and it goes back an awful long way, and when I was in Denmark recently I picked up on it again. The very first systematic linkage study done by Jan Mohr in Denmark showed linkage between the secretor system and the Lutheran blood group. That was about 1953 or something and he also had a Danish series of myotonic dystrophy families, samples given to him by a clinician, and he checked those out for linkage and there was a suspicion that there might be linkage, but only a suspicion. Now Jim Renwick had picked that up in London and that was one of the reasons why Victor McKusick was keen to take it further, and then of course things got complicated by the bust up between Jim and Victor and the lab, but that was the starting point and sure enough my work and the work that Jim was doing in London and Glasgow showed that this was a linkage, and it was the first 3 point linkage; actually it was the first time multi-point computer programmes had been used, which was highly interesting because this was then 1971 and so

AC. Not yet 'M' link?

PSH. Nothing like that, no I forget, it was Jim Renwick's programme and we used that. Most of the time we used Newton Morton's tables; you know, lod scores, which were then just quite new, and sweated it out by hand and then this computer programme would analyse three loci, which was pretty impossible to do by hand. So that worked out. The thing that was also I suppose not planned, because it required a clinical study, I had to examine all these families; I was able to collect a lot of clinical data at the same time and this allowed me to do quite a few other studies, for instance there was an endocrine study which I did in conjunction with the endocrinologists and then I worked with one of the paediatric neurologists who worked on the childhood form and I looked at all these families, and this turned up the maternal inheritance of congenital myotonic dystrophy, and so there was a huge lot of clinical stuff which then made me interested in it clinically as well as just a mapping exercise.

AC. You weren't visiting Huntington's families at that stage.

PSH. Not at all. Not at all. Indeed crammed into one of the small rooms next door was a neurologist from Michigan somewhere, who was trying to do a Huntington's linkage study but hit the big problem that almost all the people needed were dead, whereas with the myotonic families you had great big families, and so she didn't really get very far with that because she had lots of fragmentary families and so, no I mean I saw Huntington's but I didn't have a special interest then.

AC. I interrupted you. You were talking about getting a job back in the UK.

PSH. Yes. The end of the two years approached and Liverpool was off the table and so I put out feelers, I can't remember who to, and it turned out that they were wanting, there were two possibilities. There was a possibility of a lectureship in Glasgow with Malcolm Ferguson-Smith, who had now got things very well set up, was closely tied in, actually worked with Victor before, and then in Cardiff they were wanting to set up something in the Department of

Medicine from scratch. So I flew over and looked at both, was offered both and it was not an easy decision because, you know, it was between a set up that was well established, obviously going places, and something which didn't exist but you had the opportunity to start

AC. Shape it.

PSH. That's right. So I chose the second and I think I can honestly say I haven't had any regrets, although it inevitably meant things took longer and there always are difficulties if you choose the starting-from-scratch road.

AC. So was that Reg Hall?

PSY. No it wasn't, it was Robert Mahler, he was Professor of Medicine. He was a metabolic physician and a very able guy. Done a lot on glycogen storage disease. He was really more a medical biochemist, metabolic medicine person, and it was just at the time when the Cardiff Medical School had moved to the Heath from the Infirmary and was building up. They had been given a lot of money to expand the Medical School and they were trying to create new specialties and this was part of it.

AC. So you set up shop if you like, pretty well straight away?

PSH. Yes.

AC. As medical geneticist while keeping an intake, general medical etc

PSH. Oh yes, because you see when I arrived, again, the post was in the Department of Medicine and people said, well you know you've been medically trained, done a lot with Cyril Clarke etc, do you want to carry on doing some general medicine? And still at that stage I suppose I was by no means certain whether medical genetics would take off as a speciality, and I thought, well it seems a good idea to keep a foot in the door, and it might be a good way of getting links in a place where I haven't been before, so I said yes and it carried on like that as you know, for 30 years to be precise, although what I actually did was relatively small and as far as I know not too many disasters happened, but I carried on then with a small general commitment as part of the professorial unit and again that was very nice, but I don't think I would recommend anybody to do it now. I just don't think it's feasible; so I suppose I started off then, yes, within the Department of Medicine and given facilities and in fact it didn't become academically a separate department; Robert Mahler moved back to London to Northwick Park after I had been in Cardiff I suppose 8 or 9 years and Reg Hall came and was very supportive, but he was very strong on an integrated Department of Medicine, so it stayed as a sort of section until he retired, which I suppose actually must be 15 years ago, so most of the time it was not a full Department.

AC. When I was first employed it was still a 'section of Medical Genetics within' in the mid '80s

PSH. Well, actually you see, I think there were two huge advantages, because first of all, it was a section, it meant during those years when I was

building things up, I was sheltered from a lot of admin and such like, and having people like Robert Mahler and Reg Hall very supportive, that was fine. Of course it wouldn't have been fine if they hadn't been, but as it turned out it was fine. And the second thing which was also actually a help, was that cytogenetics, you see, wasn't my responsibility, because Mike Laurence had set it up as part of paediatric pathology; I interviewed him actually a few weeks ago and we went back over things, and you see he came from Great Ormond Street, where he had had contacts with Cedric Carter and set up as paediatric pathologist at Llandough Hospital and then developed, well he had already got this interest in spina bifida, and then he set up a chromosome lab; then when the new hospital opened, which was just after I came, he then a year or so later moved the lab across and meanwhile I had started genetics clinics firstly down at the Infirmary and then when the new place opened, up here. And he also developed clinics, mainly spina bifida and pre-natal. But again it meant I didn't have to run a cytogenetics lab and so I was pretty free to develop things in the way I wanted without a lot of constraints.

AC. So you saw presumably whatever was referred, but you must also have been actively looking out for specific diseases to develop an interest in them?

PSH. Yes.

AC. So what were you actively going out to look for and what just happened to come along?

PSH. Well, I think when I came back from America, I had the feeling probably myotonic dystrophy is not common enough, and certainly congenital myotonic dystrophy not common enough, to be able to make that a main research plan. But then within a few months of coming, Sheila Wallace referred me a child. I had given a talk on congenital myotonic dystrophy and Sheila Wallace came up to me and said I am sure I have seen a child like this recently, misdiagnosed as cerebral palsy. So she asked me to see this child and sure enough he had congenital myotonic dystrophy. He was about 18 months by then; I carried on then looking after him for the next 30 plus years until he just died last year. That was Gareth [ ] and that made me realise this can't be that rare; so I then wrote around the British Paediatric Association. Those days it was much easier and I sent a letter to every Paediatrician saying, have you seen any cases of myotonic dystrophy in childhood? I'm interested in this. And lots of people very helpfully wrote back from all over the country, so in about '73, I spent a large part of my time again driving and going by train all round the country, as far as Aberdeen, seeing all these and again combined a clinical and a genetic study, so the clinical study documented a lot of the very characteristic features, which weren't all new, but they had been documented as case reports and small series, but this was a series of 70 or more. Then the genetics side, almost all were maternally transmitted, so that really then put me back onto the myotonic dystrophy road again and made me realise there were a lot of further clinical things one could do and I maintained contact with a lot of these families, and then alongside that Charles Wells, who I don't know if you remember as a neurologist? He is no longer living but he was a very meticulous neurologist.

AC. I never met him, I have only seen his letters.

PSH. You would have seen his letters.

AC. Oh yes

PSH. Very detailed letters and he came along to me one day and said, again I had not been there very long, and said, oh we've got quite a few Huntington's families; I think there are about 8 or 10 in South Wales, I wondered if you would be interested? And he actually very methodically kept, any interesting patient, he kept an extra copy of the letter in a file. That was in the old St David's Hospital where neurology was based, and then when it moved he didn't know what to do with these files. He took them home and I gather kept them under the bed until his wife objected, then he brought them in and gave them to me. So I was very lucky; then I suppose this is now, it must be about 1974 or something, I got a local grant for somebody to work for a year or it may have been 2 years, as a research fellow, a guy called David Walker who was training in medicine, had his membership and between us we started seeing these families. And of course it wasn't 8 or 10, we were soon up to 100 and we realised this was a massive problem and that then launched the Huntington's work, which we realised there was a tremendous need both for family support and genetic services and so that was rather less of a research study. It was more set up on a service basis. But then the two came together when the DNA work started, and also at that time of course, as you know, it didn't start with either of those, it started with Duchenne & Becker, because I had met up with Bob Williamson and I suppose this is '78/'79. He had just moved from Glasgow to St Mary's in London and Kay Davies was with him and they were getting the first DNA markers were coming out. A really exciting time.

AC. I remember Ed Southern's paper in 1975 because I was doing my Part two in genetics and didn't realise where that was going to take it, but at least remember it coming out.

PSH. Yes, well it was exciting.

AC. Just a few years after that.

PSH. That's right. And I went up there, spent some months learning the techniques.

AC. At St Mary's?

PSH. Yes, and then the obvious condition to start with was Duchenne, because at least you have the markers coming out from an X chromosome DNA library. That was really exciting. Chromosome sorting was being done by Brian Young in Glasgow. Kay Davies was isolating probes and so these first ones came out and I think we had already started studying Duchenne from the service, in fact we had from a service point of view, using creatine kinase and things, and Jo Sibert was involved with that, and so by the time those markers came out we had a good set of Duchenne families ready to test and so that was how the DNA linkage.....

AC. So you had been banking DNA when you took blood for CKs.

PSH. No, there was no such thing as banking DNA. We had to go round and get more samples, but anyway we did that. So Duchenne was the first which showed anything that was really exciting.

AC. 128

PSH. Yes and RC8; all these completely useless things, but in fact we did, apart from a Nature paper, we did manage to get papers showing that you could use flanking markers and we did show, and that was Helen Kingston's work, that Becker and Duchenne were allelic, which of course was not what they were meant to be, because there was supposed to be linkage with colour blindness down the other end of the chromosome. So that was exciting and then we thought, what about an autosomal condition? The first thought was Huntington's, but by then David Housman had already visited, because he knew about our large families and we said we would be very happy to send samples and work with him, because he had started there with Jim Gusella helping him and so we thought, well no point in doing that separately, what about myotonic?

At the same time we were very lucky that we struck oil, in the sense that this Denver oil millionaire turned out to have myotonic dystrophy and set up a charity and advisers in terms of research, and we were able then jointly with Bob to get a grant, a large grant, to try and map the myotonic dystrophy gene and that allowed us to set up a molecular lab in Cardiff, rather than just be reliant on St Mary's, so that was set up. We also then had Mansoor Sarfarazi who had developed the linkage techniques, so we had the clinical side, the DNA lab and the linkage analysis altogether, and then the thing which I have always found amusing was, when we put in for that grant, nobody knew which chromosome myotonic was on. We knew there was a linkage group, but no one knew what chromosome it was on. There was some vague evidence that it was on, I think it might have been chromosome 7, but it was terribly vague. But we put it in this grant, because it looked a bit better to know which chromosome we would be starting looking at. Then I remember going to the international meeting in Jerusalem where somebody presented 'assignment of Complement C3 to chromosome 19.' Well of course we knew then already that myotonic was linked to complement C3, so that put it on 19 and I remember when I got back, the first thing I did was to ask whoever was secretary then, did you actually send off that grant application? and whoever it was said "Oh dear I'm afraid we've been terribly busy, it hasn't actually gone off" So we got it out, and there were no word processors then, and I remember Tipp-exing out 7 and letting it dry and then putting in 19 instead.

Well we got that grant, and so you could say then that that tied in the early myotonic research with DNA gene mapping and then the X-linked work as you well know, because you were involved with it, and then carried on I suppose from Duchenne, and then Huntington's came back on scene again when we joined in with the collaborative group, which again was very exciting and we realised we could make a contribution that other people weren't. And then it all came to a head really about '92/93, when these genes all came tumbling out. So that was an amazing phase.

AC. Yes particularly with those two diseases being triplet repeat expansions. I suppose it was just a coincidence really, was it?

PSH. It is a coincidence. It's coincidence that we were working

AC. On the two yes.

PSH. But during the later phases, I think this was one of the Cardiff contributions. We kept looking across and we kept saying to people, look there is anticipation in myotonic dystrophy and there's anticipation in Huntington's, so the research communities involved were quite separate. They didn't think there was any sense in looking across from one disease to the other and we kept on getting up and talking about Huntington's at a myotonic meeting, and then going to a Huntington's meeting and talking about myotonic, and after a bit people occasionally listened and it was very useful. Then of course once the genes had come out, there was a parting of the ways and there was no way you could go on, once the mutational work had been worked on, you couldn't really ride two horses at the same time.

AC. It moved into different fields of cell biology.

PSH. It has, yes.

AC. Other disciplines.

PSH. But they were very exciting years.

AC. I'm sure it was, yes. If you try to think more broadly than just myotonic and Huntington's, how would you sum up the productiveness of the Cardiff unit?

PSH. Oh, that's difficult.

AC. Those have been two central things

PSH. Yes.

AC. But there has been a lot more going on than just that.

PSH. Absolutely. I think for a long time we were just about the only unit that had a very strong research track coupled with a very strong clinical and service track. I suppose the interaction of the two, and being at the interface, I feel I have spent my whole career at the interface, which is often quite tricky, but I think you need people there, looking across from the service side to the research side and trying to utilise opportunities, and then trying to capitalise from your research, using that then to build up the service. For instance, having got the DNA and molecular work going on, research that put us in a good position for putting these things into service when the Department of Health started to set up pilot service labs and it was us, Martin Bobrow [actually Marcus Pembrey] and Manchester who were the first, and that really gave a boost and then again, having the regional clinics, they kind of fed in

and made a lot of sense to some of the epidemiological studies like the Huntington's survey and the Duchenne survey, and so I suppose what I have always felt is Cardiff's biggest contribution has been what you might call its all round nature rather than being just on one thing. But it's quite difficult to say really.

AC. Yes and obviously wearing the Clinical Director hat as well as Head of Department, academic hat must have been quite tricky at times but also productive.

PSH. Yes I think it got tricky . . .

AC. More recently.

PSH. Yes in the 'internal market'. I mean for many years people were quite happy to let you do what you want on the NHS side, but then of course when it got all rigid then it did become a lot more work. I don't think frankly I was ever terribly good at that but it did become more rigid. The academic and the NHS side were forced apart from each other and that did cause difficulties, yes.

AC. How about the focus on population level genetics? I'm thinking in terms of ante -natal screening, newborn screening, other possible population karyotype screening and stuff and the individual family focus that has been traditional for clinical genetic areas. I was wondering, how do you think the unit has tried to look both ways, if you like?

PSH. Yes. Well of course the newborn screening, that has quite a few challenges still and in a way come back into focus after being rather in the background for a long time. I'm always quite glad really that we didn't have an awful lot to do with the antenatal and related screening. Again that was something that Michael Laurence was very much involved with. I'm not sure he actually did it terribly well, but it meant that I wasn't and I don't think our unit were very closely involved, and I think that is a good thing, because otherwise we would have got drawn in far more to the kind of obstetric type work, which it would have been nice to have good links with people there, but I think we might have paid a big price for that to be honest.

AC. In quite a number of ways.

PSH. I think so, I have no regrets that it didn't go that way. It has never been something that I felt fitted closely with my kind of real interests.

AC. You talk about newborn screening coming back into focus now. Are you thinking about tandem mass-spec and MCAD coming along? or sickle cell and . . .

PSH. Yes and your Duchenne work. I mean people are examining it more now, aren't they, rather than just accepting it as something that has happened for a few conditions and is static. So yes, but I've not really felt myself particularly a screening type of person ever.

AC. Something that I referred to when I was giving that talk in the museum, I speculated a bit about what experiences might have led you to take a very particular interest in the broader issues around genetics, social and ethical areas and I just wondered if you had any comments on that.

PSH. I don't know. It's quite difficult anyway.

AC. Could this be you anyway?

PSH. I think a bit of it is. If I had to try and find the origin I would put it back in Oxford probably, where I was both taught and it was expected that it was very natural that you questioned everything, and ever since then I think I have been a person who has been critical, in hopefully in a constructive sense, but I was always kind of brought up with, and it perhaps tallied with my natural inclination, that you shouldn't accept received wisdom, you should always question and it doesn't matter what.

I remember when I got to London I found most of the people who had just gone through their medical school in London were very surprised by this, and I have noticed it ever since, that very few medical students do seem to do that. You have to sort of goad them in order to get them to do so. And there are quite a lot of other teachers get upset if people ask them too many questions, and I have always felt that you should just look critically at everything you are doing and not assume that you or anybody else is doing it the right way. Now whether that is a full explanation I'm not sure. It probably isn't a full one but it's part.

AC. Something that has just occurred to me, and maybe it's me projecting into you what I feel is true about myself, is that there have been particular families that I have spoken with and listened to and spent time with, who have had things to say about their own experiences, either their disease or of the medical system, which have triggered and shaped some of my attitudes and I was wondering say, trudging around the Appalachians visiting myotonic families, anything like that had had a shaping influence.

PSH. I think it has, and I think I have always had this strong feeling that if you are doing research you must couple it with providing services for the folk that you are involved with, and I suppose again it comes back to wanting to do medicine, wanting to do genetics. I have always seen the combination in medical genetics being partly service, partly research, and trying to provide the two. And perhaps I suppose, having carried on as a rather general physician for such a long time, I mean basically I have always seen myself as a doctor and tried to do what you can to help, and equally I have always enjoyed the clinical side and interacting with patients and family members and I have just always felt that is very important. But when you come to the wider social issues I guess it's always come naturally to me to question. I think that's what I take it back to in a very general way.

AC. Now there's a danger this could become like Desert Island Discs because there are a couple of questions I know, on your sheet, that I haven't covered and probably ought to. One was, what do you think the contribution

you value most has made to medical genetics in Britain. Do you think that would be....

PSH. I think one would have to say the myotonic dystrophy work, because although the Huntington's work has been very important, there have been a lot more people doing that worldwide. Myotonic dystrophy has always been a small area and I think that the combination of the research on the congenital form and the finding of the gene mutation, I couldn't pick out any single point, but the myotonic work I would feel, that's somehow where I feel I made a mark.

AC. Both of them you have taken through from the very early stages to virtually the point of treatment.

PSH. Including the genes coming out, yes. But I think yes, if you gave me one area of work I'd say the myotonic work definitely.

AC. And who do you think has been the biggest, or what do you think has been the biggest influence on you?

PSH. I suppose it would be a combination of Cyril Clarke and Victor McKusick really. Cyril for sheer genius and being the person with this vision of being able to combine genetics and clinical medicine. He was an absolute genius, and so being able to be there for those two years was a huge influence. And then I would have to couple that with Victor McKusick, because without that spell at Hopkins my horizons would have been really quite limited and Victor's range of interest and depth was also a big influence. So I think those two people were definitely the main influences on me both in terms of starting my career and really developing it.

AC. I've kind of checked through this little list in case there's anything else, but is there anything we haven't touched on that you're thinking Peter, or I should have prompted.

PSH. I don't think so Angus. I mean there are lots of details but they can be picked up elsewhere and to be honest, I think I have taken up a good bit of your time as well, and so I would think we could leave it there for now and if there is anything else, well, pick it up another time and thanks for sparing the time.

AC. No it's been very interesting. Thank you.

**End of tape.**