

## Dian Donnai



### **Personal Details**

Name	Dian Donnai
Dates	1945
Place of Birth	UK (Shropshire)
Main work places	Manchester
Principal field of work	Clinical Genetics, Dysmorphology,
Short biography	See below

### **Interview**

Recorded interview made	Yes
Interviewer	Peter Harper
Date of Interview	06/02/2007
Edited transcript available	See below

### **Personal Scientific Records**

Significant Record sets exists  
Records catalogued  
Permanent place of archive  
Summary of archive

## **Biography**

Professor Dian Donnai, nee Aughton, (b 15th February 1945), graduated in Medicine at University of London (St Mary's Hospital Medical School) in 1968. After training posts in paediatrics at St Mary's Hospital, Northwick Park Hospital and Sheffield, she was appointed senior registrar and in 1980 Consultant in medical genetics at St Mary's Hospital, Manchester. In 1994 she was made Honorary Professor of Medical Genetics in the University of Manchester and appointed to the substantive chair in 2001. She has been President of the Clinical Genetics Society (1997-99), consultant advisor to the UK Chief Medical Officer (1998-2004) and President of the European Society of Human Genetics (2009-10). She was the Carter Lecturer of the Clinical Genetics Society in 2004 and received the March of Dimes Lifetime Achievement Award in Genetics in 2010. Her main interests are in dysmorphology, genetic service development and in public engagement in genetics.

## **INTERVIEW WITH PROFESSOR DIAN DONNAI, 6<sup>th</sup> FEBRUARY 2007**

PSH. It's Monday 6 February 2007, and I am talking to Professor Dian Donnai at St Mary's Hospital, Manchester. What I would like to do first is just to start at the beginning with yourself and then go on to more general topics. But can I ask, where were you actually born and brought up?

DD. I was born in Whitchurch in Shropshire and I went to Whitchurch Infants, Whitchurch Junior and Whitchurch Girls High School before escaping.

PSH. And is it too rude to ask which year you were born in.

DD. I was born in 1945 and I was a twin. I've got a twin brother and my mother, who was only about 4 ft 9, had previously had a very premature baby that had died and so she carried us twins and we were delivered in the back bedroom by our local family GP and I've still got the bill for my birth actually, because this was pre-NHS.

PSH. So really you were only a mile or two from the Welsh border.

DD. That's right.

PSH. You must have had some sort of forays across it from an early stage?

DD. On my bicycle, yes.

PSH. So you went then into medicine but which medical school did you go to?

DD. I went to St Mary's in Paddington in the University of London. My Dad was a workman so we were not a family that had any history of secondary or certainly tertiary education and all of the other London medical schools asked whether your father was a member of the Medical, Legal or Clerical profession. So the only one that didn't ask was St Mary's Paddington, so that is entirely why I chose that.

PSH. They weren't able to ask, did you play rugby, which they probably would have if you had been male!

DD. Yes. So I was accepted there because I did my 'A' levels when I was 17. My school didn't do science actually. I had to go to the boy's school to do 'A' levels because they did botany and zoology, which was obviously suitable for a very small girls school, but not chemistry and physics. So I had to start chemistry and physics from nought to 'A' level in 18 months. I had to go to the boy's school on my bike to do that.

PSH. What made you want to do medicine?

DD. Well I don't know. It's interesting actually. I actually think there are more twins and left-handers in genetics than you would expect by chance, and actually I think that is because people who are either left-handed or a twin are a bit different and ask questions about how they are, and so I think I was

always a bit interested in that and then when I was about twelve or thirteen I went to Oswestry orthopaedic hospital because I had some exostosis on my arm and I was fascinated by the whole medical business and thought that I wanted to be a physiotherapist, and the headmistress of my little country school said that she thought I could do medicine and encouraged me, in spite of there being nobody from my school who had ever done medicine, and she was the one that got me signed up to go to the boy's school. I have never worked so hard in my life as I did for 'A' levels. It was downhill thereafter I think.

I was interested, actually I subscribed to the New Scientist when I was in the sixth form and that was at the stage at which, this would be about 1959/60, so it was when the whole of the knock-on effect of having understood the structure of DNA was being discussed and things, and so I've still got bits that I cut out from the New Scientist from that about DNA.

PSH. Apart from your teacher was there any kind of family interest? You said that they hadn't had further education but were they interested in natural history or any particular thing that might have led you that way?

DD. No, I don't think so. I think there wasn't much to do in Whitchurch in those days and the one thing that I did do was, I was a member of the Girl Guides and that was what started my interest in natural history but also widened my horizons. You know, it was a national and international organisation and it was the only way that one could, at very low cost, get out and do things and it was probably that that awakened my interest in that sort of area.

PSH. Moving on then from medical school, what was it really that took you into medical genetics as opposed to some other clinical field.

DD. OK. I got into clinical genetics by chance I suppose, as most of us did. I was interested in paediatrics and the reason I was interested in paediatrics was that there was a very good professor of paediatrics at St Mary's in Paddington called Tom Oppé and he had been involved in the delineation of the outbreak of hypercalcaemia after the end of the war, where there was vitamin D fortification of national dried milk and they had been involved with Reggie Lightwood, who was involved with that and they had then found this group of kids that didn't respond to withdrawal of national dried milk, which turned out to be the kids with Williams syndrome. Tom was nice to students, which some of the old Harley Street, London, physicians that taught us were not, and Tom was a decent man and he started the first home-care paediatric unit, so he looked at children in the context of their families, which obviously appealed to me, so I was interested in paediatrics. But I was also interested, everybody said we can solve prematurity. We can solve infection but we will never be able to do anything about congenital malformations. It was that sort of challenge somehow that I quite liked the idea of. I've still got photographs from when I was a paediatric houseman of children I saw with malformations then.

So I was always a bit interested in that side of things, but there was nothing you could do with it at that time and so I did paediatrics in a number of

locations in London, at St Mary's and then at Northwick Park the first year it opened, and I also did an obstetric job. I was a bit famous in obstetrics jobs to be a bit more interested in the baby than the mother, and so I just did paediatrics. Then my husband got a job in Sheffield so we had to leave London just as I was applying to Great Ormond Street, so I never did go to Great Ormond Street. Then in Sheffield I was interviewed for a Paediatric Registrar job by Victor Dubowitz and Ronald Illingworth and I didn't get the job, and it was the first job I had ever gone for that I'd never got. Interestingly as a little footnote, many, many years later, Victor Dubowitz, who by then had of course moved and had had a very distinguished career in London said to me "Di" he said "I've always felt guilty you didn't get that job" and he said "You know why it was. Ronald Illingworth said you were by the far the best but they couldn't take the risk that you might get pregnant." Actually I then said they did me a great favour because it meant that my career in paediatrics didn't really take off. I worked as a registrar in paediatric casualty and part-time in general practice which actually, nothing is ever wasted, so that was good. And then by the time I got to Manchester, following my husband with his career, Rodney Harris was sitting with my husband in the canteen at St Mary's one day and Paul, my husband, said how fed up I was, you know, because I'd got two little children by then and how I needed a job and Rodney offered me the two clinical assistant sessions that his wife Hilary wasn't going to take up. So that is how I started in genetics.

PSH. And then going from there, how long was it before they actually made you a consultant?

DD. Well I was started as a two-session a week clinical assistant and got my feet under the table. My kids were in nursery and we had to pay for a whole day so I just stayed at work for two whole days, and then it was at the time when I believe there were the efforts being made to set up Senior Registrar posts and three were established, one in Cardiff and one in Manchester and one in Northwick Park. Robin Winter was appointed to one, Ian Young to the other and myself to the Manchester one.

PSH. So you were one of those three individuals.

DD. One of those three.

PSH. That's quite a historic thing. What year was that Di?

DD. I was appointed as a clinical assistant on my birthday which is in February 1977 and I was appointed as Senior Registrar probably about a year later in 1978.

PSH. Because I have noticed that that was more or less when you first started publishing in genetics and I think, wasn't your first, one of your first papers was already on antenatal diagnosis as well as on syndromes?

DD. Yes, because I think being based in a maternity hospital where there's some paediatrics as well, that was the focus of some early development and we were anxious to get into prenatal diagnosis. And as I remember Rodney had already, Rodney, who was adult trained of course, had already started to

develop prenatal diagnosis and to try and zap up the cytogenetics lab, which hadn't been very good when he first came, and amniocentesis was just starting in Manchester, and so as a clinical assistant and then as a senior registrar these were things that I was very much involved with, because basically I didn't have anywhere to sit when I first came because the genetic department was tiny, so I had to lean on a counter in the secretary's office. That's where most of my first year was spent and then next door was a cytogenetics lab and I used to go and sit, if I needed to sit down I used to go and sit down in there and talk to them there. Now this was before Andrew Read came to the department but he came about the same time that I was appointed senior registrar. By that stage we had taken over next door, which was cytology, so we had a bit more room, but the labs had to go in one end and clinical people in the other and there wasn't room for an office for Andrew and me. There wasn't the space so Andrew and I had adjoining desks in the corridor but that was a great advance on having to stand up all the time.

PSH. Coming back to dysmorphology for a moment then. You had had an earlier interest, which I hadn't realised, on Williams syndrome, back in I suppose undergraduate days.

DD. There's another funny story as well from my very first paediatric job, because my pre-reg job was a paediatric job with Tom Oppé, actually and there was a child born to doctors, and the baby was clearly very abnormal and the baby died soon after I think she was born and I remember arranging for photographs and then recognising that this baby, this was probably 1968/69, recognising that this baby needed to have a chromosome test but of course St Mary's didn't do chromosome tests. So you know, everybody thought I was mad but I got somebody called Angela Taylor over from the Guy's lab. She used to work with Paul Polani and I remember her taking a skin biopsy sample from this baby and I had photographs taken and I've still got those photographs. Then I never did hear what happened because mine was only a 6 month job and I must have moved on. Years later, I wrote to Caroline Berry and asked her what had happened to this baby because I had the photographs and I wanted to know what the child had, and it turned out that child was probably one of the second or third described cases of Wolf Hirschhorn syndrome. And in fact the result had come back and that baby had been written up but the result had come back to the registrar who had never even seen the kid, who then wrote it up and so that was a little footnote to that. So I had been actually quite motivated to look a bit further even as a houseman.

PSH. What stage was it that you started linking with Robin Winter.

DD. Of course there were very few of us then and everybody knew everybody and I remember at the Clinical Genetics Society Meeting, I used to put some slides in my pocket, as did Robin, and we used to stand in a corner and look up to the light at these slides and one or two people would sort of gather around you. And he was linked in with, even though he was at the Kennedy Galton, he was linked in with Great Ormond Street, so he used to have some interactions with the people there, and then eventually of course Michael Baraitser moved from Kennedy Galton down to Great Ormond Street and I found out that they had a lunchtime meeting once a week or once a

month, something like that. So I remember talking with Robin about whether it wouldn't be sensible for us all to get together and so I think I went down – the dysmorphology club started by this lunchtime meeting at Great Ormond Street, where I would go at vast expense all the way down to London for an hour, and I remember being hacked off by this after a while and so said, couldn't we have a whole afternoon on it to make it worth my while going down. And so that happened fairly soon afterwards and I can't exactly remember which year that was, but I think that would be somewhere around 1979 when we started having those meetings, which were then just in an afternoon and people from round the country started to come, because there were lots of research registrars around at the time as well as an increasing number of senior registrars.

PSH. So, I'm very ignorant then. Was it actually Robin formally who started the dysmorphology club or were people like Cedric Carter involved at all. How did it actually begin?

DD. No. I think we didn't call it that for a bit. The meetings that were at Great Ormond Street, the lunchtime ones, were when Cedric was there and I think Anita Harding was doing a year's attachment there and there were other people around. This may even have been before the John Burn era. And then it ended up being a consensus thing so it wasn't like one person thought it should happen. It was, I like to think that the afternoon, you know making it stretch from a lunchtime meeting to an afternoon, was largely to do with my pushing them because of the travelling I had to do but that was, you know, the great thing about it, it was never formally constituted and it still isn't formally constituted and it runs by consensus and it's gradually evolved. Great Ormond Street has always been supportive of it because they provide the location for it and they do some of the photocopying and things of the case-notes, which we didn't have to start with but then subsequently we have done.

PSH. Thinking of things moving on from there, one thing I noticed in going through your papers, it goes back a long way, your interest in relations between dysmorphology and chromosome abnormalities, and particularly later the microdeletions, but also more generally, balanced rearrangements and all these other things. How did you get particularly tied in with the chromosome side?

DD. Well I suppose that was because that was all there was then. If you wanted to work out why things happened that was the only sort of technique and things that were around and I was always rather conscious of the fact that cytogenetic reports in the service lab described chromosomes that are sort of dead, because they are squashed on a slide and fixed, whereas of course chromosomes are part of a living cell and functionally part of a living cell and I always remember thinking, how could this happen? I had some kids with diploid-triploid mixtures and trying to think how you would end up having both of those sorts of things. In fact one of my very early papers was a liveborn case of triploidy and trying to work out how that would happen and the only other technique we had to investigate it was tissue typing, so we did a bit of HLA typing on the triploid cell line and on the parents.

PSH. Was there anybody either in Manchester or anywhere else really you were able to link with in the cytogenetics labs?

DD. The only person that I did originally was when, do you remember when high resolution banding came in and Marina Seabright invented that, and we introduced that in Manchester and that actually picked up quite a lot of cases that I was quite sure were things like Wolf Hirschhorn but the chromosome reports had been normal. I remember linking in with Marina Seabright and getting her recipe off her and trying to interest our cytogenetics lab in that recipe and also I was obviously going to CGS meetings and listening to Malcolm Ferguson-Smith and the other greats talking about cytogenetics.

PSH. One of the things which I've always associated you with, and it is a really important topic, is the importance of giving proper emphasis to the clinical descriptions in any papers dealing with either chromosomes or for that matter molecular abnormalities. Was this something that has always been with you, this feeling that it was rather underrated, or how did that evolve?

DD. Yes because I often used to feel that people tended to concentrate on 'Gee-Whizz' technology to sort problems out, but I always felt strongly that you've got to have doctors involved and doctors who see patients and doctors who are aware that they are seeing something that's a bit different or something that is going to tell them something. And then they have to make the move really towards the scientist and so I have always felt that clinicians' observations are absolutely key to all types of genetic research and I have continued to bang on about that my whole career.

PSH. Do you think things have improved at all? Do you think that people have actually in journals, or the basic scientist, do you think they listen any more than they did, to that?

DD. I don't know, because it's often now with on-line journals, clinical details are often relegated to information on-line if you want it, haven't they?

PSH. That's true.

DD. We may be partly our own enemies because we've tended to keep some sort of mystique. We've not taken account of the need to have searchable terms or standardised terms and that sort of thing, so I think we may be our own enemies a bit as well.

PSH. Coming on to the meetings again, the Manchester meeting. When was the first year you held your Manchester dysmorphology meeting.

DD. That was 1984, and do you want to know how that started?

PSH. Yes.

DD. Well it was all Peter Farndon's fault and two gins and tonics. After I was appointed as a consultant in 1980, Peter Farndon was the next senior registrar here and we used to go down to the CGS meetings in London and to the dysmorphology club meeting in London. And I remember it must have



been one of the 'dysmorphology one day, CGS meeting the next day' pairs, because we were staying in London overnight in the Railway Hotel near St Pancras and we were waiting to go out and meet some people for dinner, so we had a gin and tonic in the bar and so I said, I'm fed up with staying in London and I was tired because I had got up early that morning etc etc and Peter said "Well why don't you organise a meeting in Manchester?" and I said I don't suppose anybody would come you know. They just assume that they are always going to be in London. "Go on" he said "Go on". Anyway he bought me another drink and said well, I have always thought, I had this slight resentment because people in London by then had been referring to the dysmorphology meeting as 'colleagues from all over the country come to London to ask our advice.' It was like a red rag to a provincial bull, that. And so I thought oh damn it. I will try to organise an international meeting, because I think I had just been that year, or I was just about to go to my first David Smith meeting in the US, so I thought, let's have a meeting. Instead of people just having a few slides in their pockets and describing their cases, let's have people actually present work at a formal meeting.

So we had the first Manchester birth defects meeting in 1984 and I have had one every two years since then and I don't know how many people we had at the first one. Probably about thirty, and now people fight to have a place to come and we have to limit membership. Because we have tried to keep it, what I really wanted to encourage was people not just to be purely descriptive, to think about the mechanisms of underlying patterns of birth defects, but also what I wanted is, I didn't want a sort of meeting like some big meetings where people stay in different places, go off for dinner with different people, then just turn up to the meeting. You know like the American meetings. People tend to walk in and out you know, they only dip in and out of certain sessions. They really wanted it and so we have always gone for a conference centre where you can live and eat and do the work and I'm really proud of what the Manchester meeting has achieved in terms of collaboration and the sense of community in people involved in birth defects work through Europe and beyond actually, because there wasn't that forum really.

PSH. You are absolutely right. One of the things I was actually going to ask you was, I have always seen one of your roles as spreading this collaborative approach to other European countries where previously they would always hold their cards close to their chest and would n't share with other people. How do you see that as something which has evolved?

DD. I think a lot of people got to know a lot through the Manchester meetings, and some people who came to the Manchester meeting recognised that they needed to get colleagues in their own countries involved in more collaborative stuff. The Dutch obviously were early people to come to the Manchester meeting. The Dutch on the whole are terrific and have got things better I think sorted out than we have in many respects, but also having dysmorphology meetings, the informal ones, and it is interesting how other people have started it. For example Karen Helene Ørstavik who was on a course in Cardiff heard me talk and then asked me to contribute to a meeting and then as a result, she went and got Government funding, which she still has, in Norway to set up an annual dysmorphology meeting, because they haven't got so many geneticists. They've got more paediatricians, but that has

worked wonderfully. Then some Danes went to that meeting and they said would I go to Denmark, so part of my annual cycle is like a season is I always go to Oslo in August and I always go to Copenhagen in January and it has been really nice to see the community developing. I try not to call myself a dysmorphologist. I don't like calling myself a dysmorphologist. I would rather call myself a clinical geneticist with a special interest in dysmorphology. Because I noticed in the States there are quite a few people there who just wall themselves off as dysmorphologists and it's like it's almost not part of genetics or not part of anything. You know they just tend to be involved in nosology rather than actually being in the main stream of genetics and working out developmental pathways etc etc, so I have always tried to, I don't describe myself as a dysmorphologist. I describe myself as a clinical geneticist and I think that's quite important.

PSH. Yes, I would like to pick up on the US end. Before I do that though, can I just ask about France, because you've always had good links with Ségolène Aymé and yet France was also a bit walled-off linguistically for quite a long time. How did your links there come about?

DD. Well I've got two strong links really with France. I've got links with Ségolène and that's to do with provision of genetic services and information resources and that's through the excellent initiative that she started as Orphanet. But I've also got pretty strong links with Arnold Munnich's department and with other people that are involved with birth defects research in France. Also people like Nicole Phillippe and Nicolas Levy in Marseille. But quite a lot of the French now come to the birth defects conference and we've had people from France coming and spending several months in the department here. And actually Jill Clayton and I have been over to talk at their dysmorphology meetings at Necker, Arnold's place. So what I have tried to do there, and I feel that they are all part of the family actually, so I don't feel that they are sort of walled-off any more. Italy has been a bit more difficult actually. I've got links with individual people in Italy, but actually nobody from Italy comes to the Manchester meetings. So many centres there. There are so many centres. It's not sort of regional or coherent.

PSH. And they are not very good at interacting with each other.

DD. No, no, let alone the rest of the country. Although you know, I have had lots of invitations and go speak in lots of different places, but they've been more difficult.

PSH. Thinking of America and what you might call some of the beginnings of dysmorphology, who do you see as the key people who really started off the field either in a clinical or in a scientific way?

DD. Well clearly the David Smith group of people were the ones that set that off and I was a bit sort of slightly late into making contacts with them. I went to my first Smith meeting in about 1984 and didn't know David Smith at all and just some of his disciples who were there. Helen Hughes could probably tell you more about how things were for a few years earlier than that. And there were quite a lot of people who were already there established and

interestingly there were some whose approach I warmed to and some whose approach I didn't particularly warm to.

PSH. Which in particular?

DD. I mean people like Judy Hall I did warm to, because she was thinking outside the box and trying to put things together and taking big topics and she wasn't working in a pre-defined sort of framework, whereas people like John Opitz, whilst nobody could deny his immense scholarship and his scholarly approach to things, he had developed this hypothesis of developmental fields which I never understood and still don't understand, and actually now we've got much more of a handle on developmental pathways, to my mind that's what we were working towards, rather than having these 'polytopic field defects', which I never understood what that meant. So I didn't warm to that sort of thing. Bob Gorlin of course, he is a giant in this sort of field in terms of his amazing memory and also in terms of his intuition. He has got a very intuitive approach to this rather than a restrictive approach to this and you know, although I don't believe everything Bob said, I recognised very much his huge ability to recognise things and to remember them and then to document them and through his great contributions like the books and things like that. Obviously I got to know Bob very well and he was a regular at our Manchester Meetings and I used to go his meetings in the US, in fact I just spoke quite recently at his memorial meeting in Minneapolis just before Christmas.

PSH. Yes, it was amazing in a way that he had such a long spell when he was able to continue working. It was really nice.

DD. Yes, and so then there were all the people who worked with David Smith, but they were, a lot of them, the Ken Joneses, the Brian Halls etc etc, they were still adhering to hypotheses that had been developed to do with underlying vascular causes of malformations, things like that, which may well be true but you forget that anything to do with vascular development, there may be environmental things or developmental things, but it's got to be genes that control those in the first place. So you've got to look behind those sorts of things and be a bit broader ranging as well. But those meetings were very valuable; they did go through a bit of the doldrums, but I believe they have picked up again now the Max Muenke and the Les Biesecker, all of the people that have made major contributions to the understanding of malformations, have joined in.

PSH. One thing that has always intrigued me is how, at least in Britain, the paediatricians as a community haven't really got involved much with dysmorphology and it's been left to become part of clinical genetics rather than being part of the sub speciality of paediatrics.

DD. Thank goodness.

PSH. But I mean, why do you think that has happened because it isn't like that everywhere is it?

DD. No, I don't think it is like that everywhere. It's interesting because paediatrics in the UK, and this is really me looking from outside, has turned into various tribes and they've tended to be specialists haven't they?

PSH. Yes.

DD. And so there have been the neonatologists, which are obviously a good example and they've done some fairly outstanding work, partly because our health care system allows you to do those sort of big scale studies etc. and then there have been the community paediatricians that have developed their own area and then all of the other 'ologies' within there and whilst individual ones, you know, some people will turn into very, very good geneticists to do with their particular field and obviously people like Victor Dubovitz and Francesco Muntoni and all of those people you know and Gardner with epilepsy and things are all outstanding examples, nobody's quite embraced the malformation area and I think also, we might have stopped them doing it as well, because I think as genetic centres developed in each region, people who were interested in birth defects from a clinical genetic point of view, tried to integrate themselves in the team of people looking after these children and particularly in the early phases of diagnostics when the children needed diagnosing. I certainly here used to come in, was often called in by the paediatric surgeons when they had a child that they didn't know whether to operate on, perhaps one that they wondered about Trisomy 18, and I got into the sort of working relationship with these people, this was before FISH of course, where I would say, I really am sure enough of this diagnosis for it to be taken into account in clinical management, and very often with that, they wouldn't rush the child off to the operating theatre. They would obviously just do the normal supportive care and allow the family to spend some time with the child rather than whipping it off to theatre for probably half of its life. So it's those sorts of approaches, and I know Robin certainly did this. We used to go out, and we still do, and visit regional hospitals and see children in the acute situation. So I think that was how, maybe because genetics was regionally organised and became strong in many places, it seemed more sensible that it was our bailiwick rather than anybody else's.

PSH. The other factor which I've always felt must play a role is that clinical geneticists are serving such a huge population base compared with most paediatricians.

DD. And they will have seen something before. Because still many paediatric units still think if it's not in Smith it's not been described, sort of thing.

PSH. One thing I would like to ask you a little bit about Di, switching gears, is your role as a DOH [Department of Health] adviser. Are you still DOH adviser?

DD. No there is no such post anymore. I was the last of the line.

PSH. When did they abolish it?

DD. About two or three years ago.

PSH. Is that something due to you or is it just the government would not have anybody independent?

DD. No, no. I think that was the case. I think what happened was, I think it is down to the colleges. I think the colleges didn't like this system that was outside them being able to give advice to the DH. That was as I understand it. So they've abolished all consultant advisers to the CMO and I think that was partly because, if you think about it, the colleges' influence on medicine is being gradually whittled away and I think this was one area where the colleges felt that they and their committees ought to be the ones speaking on behalf of specialities and to get away with the formal CMO type advice, although I have to say that for some time afterwards the CMO and other people did and possibly will continue to ask individuals for some informal briefing or something like that.

PSH. Can you think of any single area that you feel you made an important contribution to in terms of DOH and when perhaps they actually took your advice?

DD. I don't know. There's probably not much in the grand scheme of things, but I was very concerned about and remain concerned about, how new reproductive technologies are introduced in the UK, because they are mostly done in the context of private services. Because there's legislation involved there's this daft confidentiality where you can't get back to people. You can't do studies because of the restrictions of the legislation, and then there was a stage at which there was the suggestion emerging that there was a higher incidence of imprinting defects in children born as the result of ICSI and probably as the result of IVF technologies in general. I really felt that nobody was taking much account of this and so I wrote to Liam Donaldson in my capacity as CMO adviser saying I thought this was an issue that really needed to be addressed, the whole issue of introducing new technologies without an evidence base to show that they were safe. Because this happens the whole time. They use a different mixture. They start sticking needles and overcoming normal biological gateways and I felt that there were real issues that needed addressing there, and as a result of that they set up an MRC HFEA working party on reproductive technologies and got some good people in to do that, which I think was one of the influencing factors on shaking up the HFEA and restructuring it as are they now. However, they are stuck with legislation and this is one of the issues really, and stuck with the healthcare delivery model which is largely a private sector thing and you can't do proper research, developing an evidence base, with that mixture and I fear this is going to happen to a lot of medicine.

PSH. It's something that struck me very strongly, not only over the years but when I've been kind of looking at this with a historical perspective, how with prenatal diagnosis largely developed through clinical genetics, there was meticulous recording of risks and all the evidence, whether it was amniocentesis or CVS or whatever, and how this contrasts when you move to, pre-implantation genetic diagnosis with this gung ho approach, that you can't pinpoint the evidence. It's all done on the media and very largely commercial. It's a different ethos and a very unhealthy one I think. I wish it would change.

DD. I think the other thing that I did as CMO adviser is, I was involved together with Martin Bobrow, in taking on the work of taking a national view on laboratory services in genetics, and this is obviously building on the shoulders of the SMD and other things but there needed to be a sort of recognition and then all of the things that gradually led to development of the White Paper in Genetics where I was involved in *some* of the discussions. Not enough I think, because there were bits in it that were a bit off the wall, like bar coding babies at birth, that sort of stuff and I am pleased to say it would have talked about screening for *hyperthyroidism* instead of *hypothyroidism* unless I'd seen it, and a few other little booboos like that. I'm just trying to think what other opportunities I had when talking with Liam Donaldson about genetics. Yes, the other one I was involved with was the stem cells. I was on his working group for stem cells in medicine and I like to think that the pragmatic approach to things contributed, and that report, that John Burn was also on as well, contributed in some way towards the more liberal approach to stem cell research. About to get slightly less liberal because of the anti chimaera things. But it is all down to the 'yuk' factor and people don't understand it, isn't it? They imagine some furry little fetus being developed somewhere rather than a clump of cells that tells you something about how things work.

PSH. Di I've deliberately just focused on a few things and not tried to sort of cover everything that you've done, but are there any big, or what you feel important, areas of your work that I haven't mentioned at all?

DD. No. The only thing is if somebody says, 'what are you interested in Di?' I say, I'm interested in dysmorphology and I'm interested in genetic services and I think genetic services are still an important area and I think the work that we are trying to do through our Genetic Knowledge Park is trying to plug the gaps between us delivering genetic services, and half the time most of our colleagues in the rest of medicine haven't a clue there are such things as genetic services, let alone how they are delivered, so one has got to make some impact there, but also in trying to link with some sort of public engagement work and that's where I see myself trying to develop things that are much more of a legacy of the knowledge parks in the area of making some impact on policy about genetics in medicine and how the public are engaged in this, because I think there is so much social science research that goes on where assumptions are made about what genetics is, what it can or maybe will deliver, and those are the people that make the impact on policy rather than those of us doing it and I really feel strongly that if people only knew what was possible and what might be possible and in what sort of time scale, we would probably be a whole lot better off than having the whole processing formed by social scientists who – we're not allowed to make assumptions about their field of work but a whole lot of them make huge assumptions about genetics and what genetics is and may be able to do.

PSH. Have you got any particular plans over the next year or two?

DD. Well I've more or less decided that I'm going to keep on working until I'm 65 because actually I feel healthy and I feel like I've still got some energy and I feel like I can still achieve some things.

PSH. And you enjoy it?

DD. I do, of course I enjoy it. That's why I do it. And I like travelling, I like interacting with all the different contacts that I've got all around the world. Obviously we've got a big and integrated department here and obviously as time goes on I pass areas of responsibility that I once was involved with so I'm no longer the clinical director. Bronwyn Kerr has taken that on, and the academic group, whilst I may still have a co-ordinating role, different people lead in different areas as well, and anyway there are so many re-structurings always happening in the university, you are never sure of what you are or what you are not actually. But I think my aim is to foster the careers of those people that will be leading the department, and I'm trying to support them. I'm involved with the management of the hospital trust and I care very much about the hospital in which I work and I also care very much that it's not been as integrated with the faculty of medicine as I believe it should be and I want to do anything at a senior level that I can to do that. You may know that recently we did not get a comprehensive biomedical research centre in Manchester so all of the five that were appointed are all Oxford, Cambridge and three in London and so there is nothing outside the golden triangle and our bid didn't succeed because we haven't got really a critical mass, but when you look at what investment we've had over the last twenty years, our 7 million a year doesn't compare very well with say Imperial at 60 million a year. So you had better not quote me on those figures because they may be a bit out, but there are probably moves afoot to try and do that but I don't think the University understands how the health service works, and probably the health service doesn't understand how the Universities work. They've got different imperatives and we've got an absolutely excellent Chief Executive here now, and I'm working with him and a group of other people to try and improve that sort of thing. So it's those sort of things, as well as trying to have some sustainability for the knowledge park.

PSH. One thing, coming right back to almost the beginning, which intrigues me, is the family with brachydactyly, which must live a stone's throw from where you were born and brought up, because they are in Chirk I think?

DD. Yes.

PSH. How did you come to re-establish contact with that family and then find a mutation.

DD. That was great, because that was a story that went on for years and years and years. There was a child born in Wythenshawe hospital which I was asked to go and see in the newborn period, and this chap had bad joints and he had short fingers and I was told his father had short fingers as had his grandma etc. I managed to get Dad's notes or Grandma's notes or something like that and there was a letter from a guy who was a surgeon from Oswestry and this guy had obviously done a study of this family and had updated them since Drinkwater wrote the original pedigree. So Drinkwater obviously wrote these pedigrees up. He hypothesised that they might be linked to the Farabee pedigree but nobody was able ever to prove that. Then this guy in Oswestry, I think his name was Salisbury, who by then had moved I think to Newcastle, I wrote to him and he sent me photocopies of his

presentation that he had done for some orthopaedic meeting in Oswestry. So I then tried to link our family in with that. Now I was interested in our family because this child had developmental retardation, quite significant, as well as these terrible joints and when I looked in Victor McKusick and Sami Tentamy's book there was a description of the Farabee or the families that they assumed were the descendants of the Farabee, and there was also a description of a black kindred and in that black kindred there was a child who had really bad joint problems and I wrote to Victor McKusick then asking about this family but he never replied to me. I remember when I got to know him a bit later on he said he didn't know anything about that family. Then there was, who was the woman that worked with Victor, just can't remember her name at the moment. In Hopkins. It will probably come to me in a moment. You probably get a lot of this when you are recording people when they can't remember names.

PSH. Much more than you Di.

DD. And I wrote to her saying, I've got this family but I couldn't get the rest of the family through mine because Grandma was blocking it and so you couldn't do a linkage study which would have been really something I would have loved to have done. And then later on, Liz Sweeny from Liverpool, she obviously found some more children with this through a Chester clinic, then we got together on it. Then there were the people in Ottawa who were doing a study on this and so I'd collected some DNAs and we sent all the DNAs to these colleagues in Ottawa and they found the mutation and I understand that the haplotype in our family is the same as the Farabee one, so Drinkwater was right.

PSH. That's interesting. So really showing the two kindreds were related was more through the molecular study than through the actual genealogy.

DD. Yes.

PSH. I think it's fascinating.

DD. Although there were two Drinkwater pedigrees I think. I've got them and if you are really interested in this I can dig all the stuff that I've got out about it. And I think it turned out that Liz Sweeney's patient belonged to one kindred and mine belonged to another kindred. We could never link the kindreds, but molecularly they are linked. So the kindreds were never able to be linked, and there's a whole host of people, I think in Stoke on Trent, as well that have turned out to be involved, but I think in some children and you just don't know what other genes are involved in the phenotype, some children, and I think we've haven't answered the question that I first asked is, how are these kids', this child that I saw, joint problems linked to the mutation and what causes the odd child to have severe joint problems too.

PSH. Just to finish Di, because we must finish, I've been asking everyone I see two questions. The first is, is there any particular person who had the biggest influence on you in terms of your career overall in genetics?



DD. I would probably say there's got to be more than one. Tom Oppé certainly, because he awoke my interest in both asking questions about why things happen and also in approaching things in the context of impact on the whole family, and Tom I'm very grateful to for that. And Tom also has been a very benign and positive influence on my career. Every time anything's happened to me, Fellow of the College of Physicians and then when I got made a Professor and then when I got a gong. He's always, bless him written me a letter and he's now sitting in the Star and Garter home with double amputations but he still writes little letters and I send him occasional letters. So he has been a very benign influence.

I have to of course, pay a huge tribute to Rodney, because he was the person who took me on and then supported my career to a certain stage before I became a bit more independent, and I owe Rodney a great deal for that and for his energy in starting this department and the approach that he took to that, because I don't think any of us can exist as bubbles, and it's no one person. When you look at any department it's a tapestry of peoples' professional lives isn't it? And you've got to recognise that maybe the figurehead person, they put twenty years in, but there are going to be people in the next office who have put fifteen years of their life and everybody else in it. So I think of course I've have got to recognise Rodney for all those positive things. And I guess there have been international people. I guess Bob Gorlin's had an influence, more as a sort of senior slight mentor. I wouldn't ask Bob whether I should do something or how I should do something but you know, it was great to have known Bob and to have interacted with him on that sort of stage. So I suppose those are the people that I worked with a lot. But of course there are one's friends that have influenced one a great deal and this is where Robin comes in of course, and it was such a terrible shock when he became sick and died and I felt a real, like he was my professional twin in many ways and we are certainly the poorer since he died.

PSH. The other question I've been asking everybody is, can you identify any one particular piece of work or field of work where you feel you have really made a bit of a contribution but where you can identify with, more than the field as a whole?

DD. It's difficult that, because I remember once being taken aside, by John Opitz no less, in America. He said 'Dian, I need to speak to you about a serious matter' and he arranged for me to have breakfast with him and he sat down and he looked at me and he said 'Dian, I think extremely highly of you but your work lacks focus and I think you need to choose a particular area of scholarship that you should concentrate on.' And I remember being really quite offended by this and I remember talking to Judy Hall about it, and we all agreed that it was a very important contribution to medicine in general and genetics and our bit of genetics in particular, it was to facilitate things and if you ask me what I feel proudest of, it's facilitating a whole lot of things, knowing what's going on in lots of different areas, in lots of different countries, knowing what's going on in developmental biology, knowing what's going on in genetics. I've got a bit of a butterfly mind and I love looking at big pictures and seeing how things work together, so I'm not going to answer you specifically. I'm not going to tell you one particular thing. I'm going to say

that it's the facilitation of it and stopping dysmorphology being just a descriptive stamp collecting thing, but trying to keep it integrated with all the fabulous advances we've had.

PSH. Di, thank you very much.

**End of recording**