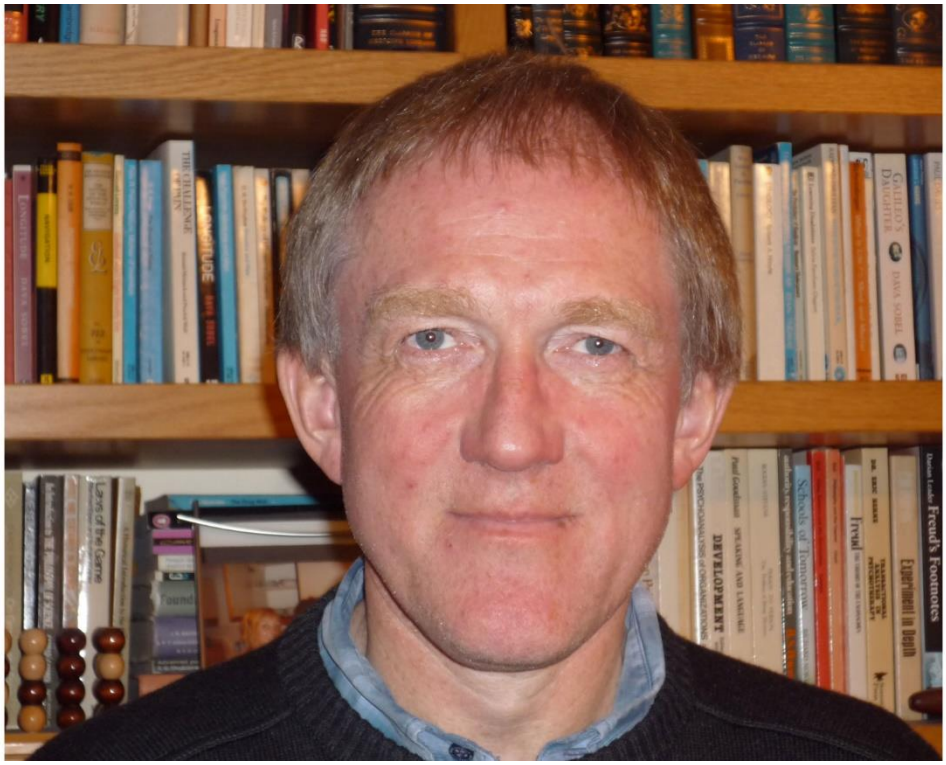
Angus Clarke



Personal Details

Name	Angus Clarke
Dates	Born December 1954
Place of Birth	London
Main work places	Cardiff, Newcastle UK
Principal field of work	Clinical genetics; ethical aspects of human genetics

Interview

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INTERVIEW WITH ANGUS CLARKE, 10th OCTOBER 2013

PH = Interviewer (Peter Harper)

AC = Angus Clarke

PH It's Thursday, 10th October 2013 and I'm talking with Professor Angus Clarke at the Institute for Medical Genetics, Cardiff. Angus, just to start off, when were you born and where?

AC I was born in London, Islington, I understand, within the sound of Bow bells, I think, December 1954.

PH And can I ask, did you come from a medical or scientific family at all?

AC A medical family, so both my parents were doctors and I never knew my mother practising. With children she stopped work more or less totally. My father was a general physician / cardiologist in North London. And my mother actually came from a very medical family but my dad did not; he had much more modest or less educated parents and family himself. But my mother came from a line of physicians and so on in Scotland.

PH That was Aberdeen if I remember correctly?

AC Yes.

PH So can I ask: was there anything in particular that influenced you in going in the direction of medicine or was it something which you kind of picked up from the family background?

AC Certainly it was always there as an interest in the family and… I suppose there were quite a few aspects of medicine that appealed to me as a teenager and so on. I think the thing actually as a teenager that most appealed, although I wouldn't necessarily echo that now, was Ronald Laing and the Divided Self and his work with David Cooper, not the David Cooper here, on psychiatric disease. And I found some of the family dialogues that they published in Penguin books and so on, to be really, really interesting and I thought I might well become a psychiatrist and that's what made me think, "Oh, let's go and do medicine" rather than maybe natural sciences. So I wouldn't maybe share that perspective on Ronald Laing now but at the time, what's amazing I suppose is that I have retained a fondness for going through transcripts and looking at conversations to try and glean what one can, what's unsaid as well as what is said, in conversations and so on. So I can see that as a continuity, you know.

PH When you went to university what was the sequence of events there? Did you go first to Cambridge?

AC Yes. So I did medical sciences, 1A and 1B, anatomy, physiology, and so on. And then I'd a choice as to what Part 2 to do, so it was a bit equivalent to the Oxford system and I suppose I wasn't sure what to do and wasn't even sure that I wanted to do a science but I did. And I became quite interested in doing either SPS or anthropology in fact, but I decided to stick with the science and it was between genetics and biochemistry and I could have done either and I chose genetics. It seemed a bit broader and more dynamic, more exciting than grinding up and doing metabolic connections in the lab. So that's when I chose genetics. That would have been 1975, I started Part 2 in genetics. So that was without any conviction that I would end up doing this in medicine; it was just an interesting science to do for 12 months, you know.

PH What was the Cambridge genetics scene then? Who was head of genetics?

AC It was run by Thoday, John Thoday, he was a Drosophila geneticist.

PH He must have been getting on a bit by that stage?

AC Yes, yes I suppose he was. Probably the most impressive figure was Michael Ashburner in the department, who has since gone on to do great things with Drosophila. But there were a number of very talented people. My recollection of mammalian genetics, or genetics, the genetics department was not on the main science site; it was on the Ely Road, or Milton Road, or anyway. But it was, I had to cycle out on the A10 quite a way battling through the trucks and things to get there because it was in the garden of a suburban house.

PH Was that R A Fisher's old house still? Because I seem to remember…

AC No, the Fishers' house was on the site that is now part of Churchill College. This was much further out than that. And the main house and annex and stuff was, but the main department with the fruit flies and fungi and things and there was a garden that looked a bit like an allotment and down the bottom of the allotment was a little shed and that was the mammalian genetics unit. And it would have happily fitted inside this counselling room. So the priorities of the department and the status of the mammals and investigative organisms, quite clear.

PH So who if anybody was doing mammalian genetics?

AC We never had a lecture from them so we were just, "Oh there's some mice down there, and it smells a bit and there's no need to visit really." [laughs]

PH And humans weren't even thought of, I suppose?

AC Clearly not. It was interesting. Quite different in Oxford, even then I think. But yeah, but that's how it was, so…

PH So I suppose you could say it was a very traditional, classical genetics department?

AC Yes.

PH And then what did you do next?

AC I went to Oxford for clinical medicine and I suppose if I had been consciously directing my career I would probably have made more effort to be part of the Nuffield department of medicine and as a student attachment and so on with David Weatherall clearly, but I wasn't particularly thinking about genetics; I was thinking about getting through and then seeing what to do next. So I didn't make any, I suppose I had my eyes open to genetics things but I wasn't seeing it as necessarily a route I would follow at all.

PH So David Weatherall, he had gone there a few years before, I guess, from Liverpool, but I don't think at that stage the Institute of Molecular Medicine was open or anything like that.

AC No.

PH And indeed I seem to remember that really to start with he was mostly haematology. And then later became Regius professor

AC I think he was professor, I can't remember if he was… no, he wasn't Regius professor then.

PH He may have been Nuffield professor.

AC He was Nuffield professor, yes. And there was John Ledingham as well there.

PH Did you have any contact with the Oxford zoology department at that point or not?

AC No. Are you thinking… Kay Davies is anatomy, isn't she? Not zoology.

PH Well it became later… I was wondering about Walter Bodmer.

AC No.

PH Okay. So you qualified and then did you stay in Oxford for…

AC I did house jobs in Oxford and then moved away,so I did a year of general medicine in Peterborough and I suppose got up to doing all sorts of things that I'm sure would be quite forbidden if you were not a senior tratneethese days. So I did quite a lot of procedures and enjoyed it but I think I was planning to maybe just slowly do my own rotation and end up perhaps in general practice, and it was a bit vague, so I thought the next thing would be paediatrics so I went to Manchester and did paediatrics. And actually she wouldn't remember but I met Di Donnai on one of the special care units. She came up to see a baby and so that was my first ever contact with clinical genetics and this was Di coming up at the end of some busy day for her, probably having a look at this baby we'd asked her to see and saying, "Oh 5p minus" and walking out more or less, but you know clearly very skilled. So that was quite interesting to see but I was quite interested in neonates rather than the genetic aspect of it. And then I went to Bristol after that to do more neonates and did nine months of neonates there and then came to Cardiff as registrar in paediatrics and worked with Jo Sibert and so ended up starting going to the muscle clinic now and again and seeing Duchenne and so on. And Jo suggested that maybe the next job I'd do should be research and he knew I had the genetics degree, so he said, "Why don't you go and see Peter Harper and see if there might be a project that you could fit into." And it wasn't quite like that; it was more going to see you and you thinking, "Well what could be tackled as part of an MD over a couple of years?" So it wasn't a project that I slotted into, it was more, "Well let's see if there's a project we could put together." And I remember we thought X linked disorders would be quite good because in a shorter time one could do linkage more realistically for an X-chromosome condition and so we were thinking between Vitamin D resistant rickets and ectodermal dysplasia. And for whatever reasons we chose the ectodermal dysplasia.

PH So what year have we got up to now?

AC Well that conversation on planning what to do, I'm not quite sure because it would have been before, but I think it was late June 85 I probably started here. Started 85/86 and then went to Newcastle 87/88.

PH So the molecular side of things had got going by then?

AC Yes.

PH And indeed I think this building would have been open just about, maybe not quite.

AC No, no. I think I didn't come into this building until I returned in 89.

PH So the ectodermal dysplasia, I mean little did you think that about 30 years later you would still be involved with it. I guess that's the case for a good few of us. But what did you start off then doing with the ectodermal dysplasia?

AC Acertaining cases, I did a lot of that before actually, well while I was still working with Jo Sibert, just doing large mail shots out to all the paediatricians, dermatologists, hospital dentists and so on, that we could find in the medical directory.

PH That was across the UK?

AC Yeah. And also that was tedious and slow. I forget about ethics, whether there was any ever ethical requirement. Maybe there was, maybe there wasn't but I'm sure if there was, I did it but I just can't remember now. I don't remember going to a committee but…

PH People were very generous in terms of making their patients available, weren't they? You know, I can remember that with my own work. People would really, it was amazing, just by writing and being prepared to travel around the country how many patients with a relatively rare condition one could accumulate.

AC I'm sure it would be much harder at multiple levels now, not just the governance, and R&D in particular, I think, can be very obstructive. But also I think consultants' knowledge of their patients, it might be more difficult for them to recall individuals, unless they had a database, unless they had a computerised diagnostic index, I think it might be harder to get people to remember the patients that they could introduce you to.

PH That's sad actually, isn't it?

AC I think it's true. I think that's the impression I have, maybe I'm wrong.

PH So at the time you'd written around and travelled around I guess a lot. How many families did you end up with?

AC If I was still counting I don't know, it would be well over 100. In the main cohort that I recruited in those near two months or leading up to and then the 18 months that I was doing it, just about 70 index cases. So quite a bit more than that in terms of affected individuals because a number of the families were quite large. And so I spent a lot of my time driving around the countryside and wrapping up blood samples and taking them to railway stations to get them transported back to Nick Thomas and his lab technician, Kim, at the time, and that worked quite well. And I had an education in the motorways of Britain, and sometimes I think it's a bit like the Road to Wigan Pier because it introduced me to some very nice areas of Britain but also some really impoverished districts, sort of urban estates and Hull and Scunthorpe, lots of places. So it probably, I don't know if I needed my eyes opening because I'd already worked in Manchester and seen quite a lot of the country but it certainly it would have opened my eyes if they hadn't already been opened to desperate social conditions and I was really very impressed by how welcoming many people from all works of life were to someone taking an interest in their condition. And a lot of people clearly had a story to tell and someone visiting who wanted to know about their condition was just, I received a torrent of information. And of course I captured what I saw as relatively medical and important and I personally remembered lots else but didn't systematically record it. I certainly wasn't tape recording people on those visits. But I was very much impressed both by the health and medical consequences of the condition, but also the personal impact on them of looking different and so what they had to cope with just walking down the street and things like that.

And I think that's true for a lot of genetic conditions where people either look or behave a little bit differently. Some people carry it off very well and successfully but a lot of people struggle with managing their appearance and other peoples' reactions to them. So I suppose I learnt a lot about that.

PH I think that doing home visits gives one a pretty unique insight that you just don't get if you are seeing people exclusively in hospital or clinics. I think that goes for most conditions.

AC I'm sure.

PH And again I'm sad that I don't think medical people coming into clinical genetics perhaps have that so much now. Maybe they do but…

AC Well I can think of one of the registrars now, Andrew Primrose, is doing home visits as part of a research project. The others aren't very much as far as I'm aware. You know I think it's something that is a dimension, that it's a shame if it gets lost. And I suppose part of it is the era of large linkage studies has clearly gone and one might occasionally need linkage but it's much, much less necessary. So I suppose it's the linkage studies where you're trying to track down affected and unaffected and everyone's grandparents and children that really motivated and meant you really had to drive and find people; because if you're only seeing or perhaps quite often seeing someone with an autosomal dominant disorder, a lot of the gene finding now would be on new mutation dominants that the need to do a big visit around half a dozen membersin the same family just doesn't exist now.

PH Did you try and do any carrier detection tests during your home visits or was there… [laughs]

AC Yes, very much, yes. I must, well I must have talked about this with you, or you've heard me present it.

PH Tell me again; my memory's awful.

AC Well I just imagine it's a motivated question because that was quite a part of what I was doing and it was at times quite amusing. And so the female carriers of ectodermal dysplasia will often miss a few teeth in either dentition and sometimes in both dentitions but some of them show nothing and some of them have major, very obvious dental gaps. So teeth is probably the first thing you'd look at to assess this in a woman. But there was a, people had described other ways of identifying female carriers and you can sometimes just from a general look if they show it quite markedly in the facies and hair. I tried to look at sweat pores on the palm and the finger pads but in fact I found that very difficult to be objective because people, maybe particularly women, I don't know, wear away the ridges on the pads and so make it quite difficult to interpret if they're doing manual work with their hands and so on. So another technique that had been described was starch and iodine sweat test on the back and so when I was doing this, you know painting iodine and alcohol on the women folk of a family who would have to crouch around the family fire and hope there weren't too many draughts to cool them down, they'd be having to get themselves hot, stripping their backs and be drinking cups of tea to help get the sweating going. And you can probably imagine if you had two, three, four women crouching around the family fire, naked backs and drinking cups of tea it brought a certain intimacy and humour to the whole affair. And I could still imagine there might be clinical applications for this even now. I mean we don't like to perhaps, but if you've got a woman who's showing quite a bit of hypohidrotic ectodermal dysplasia and you haven't found a mutation on testing and you want to know whether it's X-linked or not then it would still be quite a good way of doing it. But I can't remember the last time I felt compelled to do it. It goes back quite a few years.

PH Coming back to base now, you sent all the samples in, DNA was isolated. Remind me, at the point you were starting off this study, what hints had you about where on the X chromosome it might be a good idea to look?

AC Well there was Peter Cook at his time at Newcastle, the first HGM meeting I think, not long before his death, in a car accident, wasn't it, I think? I never knew him but I think it was in a car crash.

PH I had thought in fact he had collapsed suddenly with some kind of vascular catastrophe but I'm not sure.

AC Okay, so I'm not sure at all but he had reported a woman with an X autosome translocation and the X break point was XQ13/Q21 and so that was clearly the point to look and the question was what of the available probes might be close to that? So cytogenetically people knew where to look because of which gene finding markers were closest. So there were quite a few markers assigned to the long arm of the X but the linkage relationships between them all were not very well known and so we started off with a panel of markers and gradually got closer over the next couple of years. Of course as soon as I left Cardiff at the end of 86, beginning of 87, Jon Zonana came and it was very lucky actually, the way he had an interest in the same condition, to bring more samples from other families to join in and continue the linkage study and that went very well. And of course he tracked down the cell line established from the patient that Peter Cook reported because the fibroblast cell line had been established from that. And Jon Zonana managed to track that down and he published a nice paper on that, you know, it was useful but interesting.

PH Was it two years before you went up to Newcastle?

AC Eighteen months; I started in summer 85.

PH But during those 18 months you were also involved with Duchenne and other X linked things to some extent.

AC I did muscle clinic and I maintained one of the registers, and I forget whether it was the Duchenne or Becker register. It might have been Becker. And so I was doing that in linkage days because the publications from Lou Kunkel and so on coming out in 86 really, so deletion testing just coming in around the time I was leaving. So most of the time I was there without even, so that would be for diagnostic purposes, but for carrier detection dosage was still pretty shaky and wasn't being used immediately just then. So carrier detection was still a combination of pedigree, creatine kinase and then linked markers.

PH And Bayesian risk!

AC Absolutely. So Mansour Sarfarazi was the guy who taught me that and Alan Emery's book of methods, Methodology in Medical Genetics sort of taught me Bayes and how to come up with prior risks and posterior and so on. So that was very useful and a good way to learn, you know, to learn all that and that meant that when I was doing linkage studies with the ectodermal dysplasia results I had met all the concepts before and so that was very helpful in terms of preparing me for the research as well.

PH Then you went up to Newcastle and how long were you up there?

AC Two years. It was meant to be one year and towards the, I had applied while I was still in Cardiff, I'd applied for a job in Penang, no Kuala Lumpur actually, because at least at that stage when I applied I thought I might be able to do tropical paediatrics for a bit, and applied for a job in KL and heard nothing more from them so I got this job up in Newcastle. It was a two year job but I said I'd go for one year and then perhaps go out to KL if that came along. And it did actually but by the time, it was well over a year, it was 15 months or more, that they got back to me and said, "Oh yes, we could take you." But at the time Jane was about eight months pregnant and so we stayed in Newcastle for another year instead of going out at what I think would have been quite a tricky time.

PH And what did you actually do in Newcastle?

AC Two, three things, four things actually. The excuse for employing me was to set up and run the Duchenne register there so I spent a lot of time driving around the northern Region visiting families with Duchenne. But that was as much, probably more a diagnostic service and getting samples for linkage studies to be of practical value to families rather than primarily research. And so it was a Duchenne register. I did paediatric neurology outpatients with David Gardner-Medwin, not just muscle disease but other things. And that's when I met some Rett syndrome patients actually at the paediatric neurology clinic and genetic clinics in Newcastle but also around the Northern region so in Carlisle and Darlington, Whitehaven and so on. And I was still doing paediatric on call so I was second on call would have been for general and neonates for a bit, so I carried that on while I was doing the job there.

PH Had Derek Roberts retired by then or was he still there?

AC No, he was still there and technically he was head of department. So he wasn't head of the NHS service. I think John had, I think John was sort of running the NHS side but I think Derek was still head of the university department. And there were was a certain amount of tension and so on because they were just very different people and approaches and priorities.

PH So when you came back to Cardiff, remind me, was this to a research post or to a formal genetics training post?

AC It was to a consultant post.

PH My memory is so bad!

AC Oh, a senior lecturer post. And I'm just so grateful actually at how that job was set up because it was 100% NHS money but channelled 100% through the university and that would never happen now. And I think I found that slightly anomalous position quite helpful over the years.

PH Yes. That does bring things back to my memory because -

AC I don't know how you managed that.

PH I got into terrible trouble. I may not have told you that, because I was under the impression that if I felt one would be likely to attract a better calibre of person to the post by making it academic I was entitled to do that. And for some reason it went all through the machinery without any trouble and it was only afterwards that I think the people in the then Welsh office realised…

AC That it was anomalous.

PH That it was anomalous and I took a lot of stick for that. [laughs]

AC Well thank you for taking the stick.

PH But I think they soon relented and I genuinely I think I hadn't realised I was breaking any rules but yes, I'd completely forgotten that until you had mentioned it. Had you by then done your MD thesis?

AC Yes. I'd written it up or finished writing it up in Newcastle and I had my MD, or did I have it? I'm sure it had been passed but I might not have collected it as it were, when I started. Yeah. I don't even think one could have got a senior lecturer job without one's thesis submitted.

PH No, I'm sure you're right.

AC I forget the exact timing.

PH And thinking now about you being back in Cardiff and the X chromosome, I mean you were still very much focused on the X chromosome. I suppose focused is perhaps the wrong word because there's an awful lot on the X chromosome but I mean you were very much involved with X linked diseases and a number of types?

AC Yes, I was doing some work, there was a fragile X project in the lab and so I ended up doing quite a lot of work with some of the fragile X families to feed into that. And I was quite involved with and maintained an involvement with Rett syndrome families and so on.

PH How did that start? You mentioned a family in Newcastle but how did that develop?

AC There were two sisters in Newcastle who looked like they had Rett syndrome and one of them had pretty classical Rett syndrome; the other one was a little bit milder but with a bit less regression so without the older sister having it you might not have got to the diagnosis. She had some features that suggested it. And that didn't fit into the usual pattern of Rett syndrome and in those days people imagined Rett syndrome was an X-linked, male lethal dominant disorder probably a bit like IP or one of those group of conditions. So to have sisters with it and no one else in the family, those families, it looked as though they might be quite helpful in terms of mapping the condition because just to look at what bits of the material X they shared. Because if, as is the case usually, it came from dad of course there'd be no way of mapping it. So I put quite a lot of effort into tracking down other sister pairs and beginning to do linkage studies on them. And with hindsight it was mostly a waste of time in that it usually is paternal origin and so on. But it felt, it seemed like all one could do and what was particularly interesting about the Newcastle family was that both of the girls had metabolic anomalies as well as Rett syndrome and really very marked, which happens in patients occasionally. We did go past ethics, we did them and some other Rett syndrome patients up there. We did intravenous alanine infusions and overnight fasting and then giving a carbohydrate load or a protein load and tracking their responses. You know we had, post glucose load, a lactic acid of about 10 which is enormously high and orotic acid excretions are really very high in the ornithine transcarbamoyltransferase deficiency ballpark. So I think it is an underinvestigated, I think it is still a relatively badly understood element of Rett syndrome.

PH At what point was it that the actual mutation and gene became clear for Rett?

AC That was 1989. No, sorry, 1999. So it's just since about 2000 that it's been known as MECP2. So I suppose having worked on linkage studies in quite a number of families and having samples from quite a few just sporadic cases it meant that once it did come out we were able to get off a mutation paper follow up paper quite quickly, and that was quite nice.

PH And really the Rett work has blossomed a lot in more recent years too, hasn't it?

AC Yes, around 2004/5/6 we were doing quite a lot and that was very constructive. It was with Hayley Archer and she focused particularly on the early seizure subgroup and CDKL mutations and so I think that was all very good. Since then there have been quite a few things I've been wanting to do but have not been successful enough with grant applications. I feel we should have been doing clinical trials at the moment. There are quite a few candidate treatments and good people to link with in Bristol are doing basic work with Rett syndrome [mice 0:49:44] and autonomic control of breathing and so on. So I think there's lots to be done and together with that group I need to become more successful at the grant-writing business. But there we are.

PH One thing that's always struck me, Angus, is that a lot of the things you have worked on, a lot of the conditions, have involved fairly fundamental concepts in genetics where one has to take the concept and marry it up so to speak with the disorder. Obviously X chromosome inactivation, but imprinting more generally. I've always felt that what you've done has illustrated how important clinical genetics is if you join it up with what you might call insights into the basic biology.

AC I suppose I'd hope so and I think my, or perhaps my genetics degree from a long time ago put me in a good position to pursue interests like that when I came across them. But I couldn't claim that it was all by design; it's more maybe I was able to spot a few things as they came past rather than designing a career from the beginning, which some people do but I didn't.

PH Can I switch gear a bit now and ask at what point did you start to get not just interested but involved in studying the social and ethical aspects of medical genetics?

AC It was while I was still up in Newcastle that I went on a counselling course in Guilford, just a short one you know so I wouldn't say I had or have any huge expertise in that. But it gave me a vocabulary for thinking about how people interact in a consultation, in any conversation really, it gave me a vocabulary for that and I think that's quite crucial to, if you are trying to step out of the consultation or conversation that you're in then to have a vocabulary to describe what's going on is very helpful. And I think it allows you to step back out more easily. So that helped and having a bit of a vocabulary helped. And I suppose there were developments in genetic screening programmes which were happening around then which I had mixed feelings about a bit. And when I came here of course I had a supportive environment to think aloud about issues which I wouldn't have found everywhere. So I did think aloud about things sometimes in print, I sometimes had quite hostile reactions and responses from colleagues in other parts of the country. [laughs]

PH I remember those. And I remember that some of those people had a mental image of you as quite a different person from the one those of us here had. And that for many of them it was the first time they'd stopped and thought about the issues.

AC Yeah. I mean I remember writing a paper on I think, now which way round was it? But I wrote, I think there was one I wrote on audit and that didn't have very much response so I thought it should have provoked a lot of people and I think they sort of ignored it. And this was just saying if you drive a service by trying to maximise whatever it is you're setting up as your goal you can end up in completely unacceptable territory, so if you follow things through too logically and consistently to achieve the outcomes that you're holding up and you're presenting to funders as justification for the service, if you drive that to the maximum then the tail will lead the dog and you'll be achieving things

that you don't want to. So maybe that wasn't framed in a sufficiently engaging or provocative way. So I then followed it up with the non-directiveness in genetic counselling paper, and that's what provoked a lot of interest and I was pleased with that. I remember one amusing instance, Rodney Harris was visiting here once and we had met and you know we were perfectly polite and everything but you he was someone who didn't initially take to what I said and he had a hearing dog. And we obviously knew each other well enough by this stage so that he was out on the green somewhere with his dog and he saw me and it was just a little dog, so he sort of stooped down and said in a loud whisper so that I would hear. He pointed at me and said, "Kill, kill, kill!" So I thought that was quite nice; that was you know it was done with good humour. And anyway, so it's nice little anecdotes like that. So the hostility didn't last too long or become too problematic. But I got a response.

PH Another one I remember is the discussions over hypertrophic cardiomyopathy.

AC And the childhood testing issues, yes. And yes, and obviously that has evolved a lot as much more is known now than then. Although even now there's still a lot that's not known. But the whole childhood testing thing I think I've felt for a long time it was very interesting and it has remained so. It has remained a live issue. So some years ago on the Human Genetics Commission people were talking about what area should we look at, and that did crop up. I don't think I mentioned it. One of my colleagues who is also on the HGC said, "I think that's all sorted out and done, you know" but that's very much not the case and I think even without genomic developments I think there's still an awful lot to be learnt about how to manage some of the family issues surrounding genetic testing in children. But with genomic medicine coming online and available so generating lots of information about children that hasn't even been sought. I think the ways to manage that really need much more work so I think although this whole issue was raised back in the late 80s now, you know I think it still needs a lot of attention.

PH One of the things that's always impressed me is how you've managed to bring in a lot of the social science folk, particularly the ones here in Cardiff, philosophy and communications and a good number of other departments. But you've managed to alert them to a whole lot of issues which to be frank they weren't really at all aware of for the most part. How did you manage to get involved with them?

AC Well I suppose as far as reading Ronald Laing I used to read quite widely in anthropology and social sciences as a teenager and so I've always had an interest in those areas. And so when I saw that then some of that expertise could be helpful in genetics, I also saw that genetics could be of interest to them. You know I saw it very much as a quid pro quo that we might learn about our practice and how to think about things from having someone from a different perspective come and look at us and talk about what they've found. So we might benefit from that but so might they benefit, because if you're interested in things like family communication and decision making then having a topic like genetic disease or genetic testing or whatever, dropped into a family then provides something whose impact one can study and thereby learn about how families make decisions and how one family then communicates to another and so on. So it's very much, or should be very much a two way thing, and with some of the people I've collaborated with it has worked. I wouldn't say it's been a great success with all of them but certainly with quite a few it has and I suppose I've found myself wearing both hats in that I'm interested in what we can learn when people look at us from the point of view of improving practice and understanding what we're doing in clinic. But also I find what they're doing in terms of using genetics as a probe to dissect social processes, I find that academically interesting as well as of practical interest to us in clinic. So I find myself very much wearing both hats although I'm clearly only qualified in the one. And I find the ideas interesting.

PH You say you're only qualified in the one but you did have some Wellcome support for social science training, which I'm never quite sure what you actually did or what that consisted of?

AC Yes, well some of it consisted of employing Heather Skirton so that she could come and run the MSc for the first two years, and that probably isn't what the Wellcome Trust were meaning. I don't know because I would have been doing it otherwise so it did free me up in that sense and that's what it was for. But that's one of the things I think it achieved. And it also meant I could go around the country and carry out interviews with mostly ectodermal dysplasia families, and in fact after Heather and Clara Gaff left the MSc course I then had a frantically busy few years running it without support so that held me up massively in terms of publishing the social science type work but that is beginning to come out now so… That's quite a long time ago; I'm really pleased that I am getting on with the publishing end, yeah.

PH I mean luckily, one thing that I've realised is that people on the social science side are used to delays of…

AC A decade.

PH That's right. Even for a book review it seems to take five years or so before it gets published so… but I mean you've had some pretty impressive record of books as well as journal publications, haven't you?

AC Well of course one of them with yourself, Genetics Society and Clinical Practice and certainly some of those chapters, and some of those that we both did, haven't really been superseded and they clearly won't refer to all the latest articles in some but you know…

PH The issues don't go away, do they?

AC They don't go away and sometimes there hasn't maybe in all of those, in some of those areas there hasn't been that much movement since. So there's some quite a bit antiquated really I suppose. Yes, I did that book, on childhood genetic testing and one on cross cultural aspects of genetics where I was trying to get anthropologists and social scientists interested in genetics as a programme for dissecting social processes. And I think it did achieve that a bit and certainly yes, quite a lot of these things actually, as well as having a worthy academic goal like that some of the meetings maybe I've arranged have also been thoroughly selfish in I've arranged meetings and speakers and stuff that I want to hear, you know. So to some extent I've been very lucky in being able to get enough support to set up events that I want to be a part of it. That's fair.

PH Thinking about your interactions with the social sciences world, do you feel that you've sort of been involved then with a very different sort of culture by comparison with what we do in medical genetics and perhaps medical things more generally?

AC Yes, very much. I mean the academic world in social science or communication is very difficult; they are very different. So it's not just one, it's several different worlds if you like, and so you know it's certainly looking at a communication scholarship as one area and bioethics applied philosophy as another and social science in the ethnographic sense of describing social occasions and relations and so. I took on those quite different worlds, they're different from each other as well as different from medicine. And what is an acceptable way of behaving to colleagues and routine, yourself and everything else, the rules of engagement I think are quite different in those worlds.

PH Do you think there's a kind of reluctance at times to recognise and acknowledge other disciplines by comparison with one's own? It's something I've been struck with interacting with historians but I sense that many people in the social sciences are quite reluctant to accept the views and even the standing of people from outside their own discipline. Maybe I'm unfair?

AC How would I put it? I wouldn't put it in quite those terms. If you think from within medicine of how social sciences, psychology and some are viewed I think there is a flip side. So quite a few people in medicine would, who would want to make use of a social scientist or health psychologist, whatever, in a very instrumentalist way of maybe feeling that they have to attend to the psychosocial or ethical

side of their area and they've done this, they can tick a box saying, "We've employed someone and published a paper on it. So that's okay then." And the person who's done, the social scientist or psychologist whose done the research might feel that they've been very constrained with what they're able to say and do and they're being controlled. So there's at least some bits in this of taking advantage of sort of medical authority and academic seniority and things like this to, I guess to, almost nearly exploit someone coming in from another discipline who loses their independence. And I think one can also see it in terms of seeing the other way around in that we look and see people from social science community seeing people, seeing medics as people who can give access to data from their point of view, and they want, they might want to come and get their data and go and do what they will but some of them will be reluctant to engage constructively with the topic area. And I feel it sometimes discussing it where this as a sort of smash and grab raid, almost a sort of being treated as 'we'll get a bit of data and then we'll go and do what we want with it" without maybe any real understanding of what's gone on in the event/conversation whatever that they are witnessing. And of course they produce things that might be academically amusing within their own field but which aren't, are not really seriously engaged and don't really make much contribution I don't think. So I think when you find people from other disciplines who are willing to seriously engage with the topic area within medicine and get to know it and build a relationship around improved understanding of that area then I think that's to be cherished and to be worked at because it doesn't always happen. So that's not quite answering the question as you asked it.

PH It pretty well is and I think one thing we've both found is that forming these links requires a lot of work but in the end it's very worthwhile; one ends up with what is perhaps quite a small minority of people in the field but those people who are willing to really collaborate truly, it's very valuable.

AC Yeah, absolutely.

PH And perhaps in my view it's just a shame that more of them aren't willing to do that. But yes.

AC Yeah.

PH One thing Angus I'd like to come back to and that is your genetic counselling MSc course. How did you get the idea of starting that?

AC Hm. Well, I'm not sure about the idea but in terms of the motivation, I recall both when I was here in the mid-80s and then I recall, maybe that's the key thing, in the mid-80s I remember the group of co-workers as having a real buzz to them and a lot of accumulated insight and wisdom and commitment to really do the best for the patients they came across. And I remember them as a very mixed bunch so people were in social work, nursing, biological science graduates, one or two psychologists, so quite a range of different people. And there was something, a bit like a melting pot somehow, they supported each other and the junior medical staff like myself, and they did a big, big contribution on the service side and the research. You know and there were social work people as well so there was a big bunch of people and what I then saw over time, so this would have been I suppose during the 90s, I saw things changing and it becoming, or the groups of workers becoming professionally much more narrowly based in nursing and nurses had a lot to offer but I think I felt it was better where it was not so nursing dominated. And I think that's what made me think, "Well let's maybe set up a course that would allow people from a non-nursing background to enter the field." In a sense probably it has been too successful in that, though there still are quite a few nurses about in genetic counselling in the UK, there are a lot fewer and I think we must do more to make it, to help nurses get into the field by dipping in and out of the MSc courses or just learning approaches or some other way because there's a danger it could become too dominated by MSc graduates with a predominantly science background and without the nursing experience, and I don't want that either. Yeah, so we're not in a stable, steady state that I regard as satisfactory. We've been sort of swinging a bit. What I think is really helpful is to try and have a mix of people who can cross-fertilise.

PH When you were setting it up, I mean in this country the Manchester course was the only other one going, but there were developments in America some time before which were very different.

AC Well Manchester of course was set up by an American graduate so…

PH That was of course Lauren…

AC Lauren Kerzin Storrar. They were very helpful in supporting us early on. So we were indirectly a descendent of the North American system but professionally they're rather different for several reasons. I mean partly because they have genetic nurses and genetic counsellors as quite distinct groups and partly because quite a lot of what genetic counsellors do in USA would be done by midwives here in terms of the serum screening sort of discussions and what we would regard as more routine midwifery antenatal care. In this country genetic counselling has always been more focussed on the work of clinical genetics departments and serious genetic disease, if you like, high risk situations rather than population risk antenatal stuff. So the situations of the professions here and there I think are very different.

PH Just give me an idea of when it started; what year was that?

AC 2000, the first intake.

PH And how have the intakes gone in terms of numbers?

AC We started off with about five I should think; five or six. And it built up slowly to an annual intake of 10 students and we're limited by the number of clinical placements that we can arrange. And probably it would be difficult to go to more than we are and I think as a group of students it functions well at about that sort of size. Yeah. And it would become unsupportable in terms of either clinical placements and jobs afterwards you know if we went up to twenty. The university would love us to increase the size; we're so oversubscribed that we easily could in terms of accepting people but it wouldn't be at all fair to do so, yeah.

PH And in terms of background, what's the breakdown for background?

AC Most people are fairly recent science graduates, so most applicants have done a biology or genetics degree maybe a couple of years before they come on the course. And so it's a bit like applicants, people we accept tend to have done non lab people-based work before we take them.

PH So in terms of an aim and image do they still see themselves, at least at the beginning of the course, as basic scientists or do they see themselves more as people working with people rather than science?

AC Well they come in having done a science degree but having clearly made a decision that they want a people-focussed career and we wouldn't usually take someone who's in a laboratory and who has just made that decision. We want someone to have acted on it and done a fair bit of people-type work before we accept them just so that both we and they are confident that that's the right decision for them.

PH What about people with a psychology or social science background? Do you get some of them?

AC We've had a few. We've had someone with a law degree, someone with a philosophy degree. Quite a few nurses and midwives and one or two health visitors. But the big majority now would have the genetics or biology degree, yeah.

PH And as far as gender goes, almost exclusively female?

AC Yes. I mean we've had quite a few males actually, this intake we've got two which is good but yeah, the balance is very heavily female dominated.

PH Do you think that's a good thing?

AC [laughs] In what sense, Peter? As an employer, if I was a future employer would I want my workforce to be predominantly young women going off having babies?

PH Well I wasn't thinking of that so much as…

AC No I'm sure you weren't; I was casting aspersions.

PH I'm thinking in terms of how the character of what is becoming the speciality or the profession is forming.

AC I think it is such people based work that I'm not at all surprised that that's how it works out and I can see in a class of students studying biology or genetics, I could imagine that the go-ahead successful people from the course who are male might be more likely to want to stay in the lab than the good students who are female. And I suppose it's just similar in that sense to nursing or physiotherapy or a lot of people-based professions are predominantly female so I don't think it stands out as different from them particularly. I suppose what is a little bit different actually it's more like the clinical genetics community, actually not so much here in Cardiff but in many centres some of the people coming into clinical genetics are predominantly female too. So that means we have this, both the medical and the non medical people are predominantly female. Whereas medical students who are doing it are roughly 50/50, so in other areas of medicine the sex ratio is more even but for here the non medical and the medical group tend to be predominantly female. So maybe that alters the character of the department a bit?

PH I was interested that earlier you were saying that there hasn't been any problem with people coming out from the course finding jobs. What kind of jobs are they getting? Are they mainly within medical genetics centres or are they sort of scattered around or self-standing? How does that break down?

AC I mean the big majority either get trainee genetic counsellor jobs which tend to be sort of two, two and a half years in duration and they then have to apply for a substantive post, or they get substantive posts as genetic counsellors in the NHS centres and they'd often get Band 6 jobs and then when they achieve registration with the AGNC registration board then they might be made up to Band 7, depending upon the details of their contract. That looks as if that's the sort of pattern that most people go to. We get a few people go and do PhDs straight from the course and one of them has actually just finished, just handed in so she'll be having her viva in a month or so. And so and that's, she's instantly picked up another job, has another job elsewhere. There's just one or two people who have done other things but that's not because they couldn't have stayed in genetics; everyone who has wanted to has been able to.

PH That's encouraging.

AC Yeah.

PH One of the things which has been quite recent and I really don't know much about but I mean as the genetic counsellor grouping has become increasingly professionalised and with its own organisations, I've gained the feeling that in this country that's all been pretty positive and harmonious in terms of relationships with medical geneticists and other groups. I don't get the feeling that it's been like psychologists and psychiatrists with an us and them grouping. Now maybe I've just not been aware but how has that been do you think?

AC I think what you say is true within this country as Wales. I don't think it's, I don't think it's completely unproblematic if we go around the UK as a whole. And I think patterns of working are very different, suit some people more than others. So there are a lot of centres now where patients will tend to be seen either by a genetic counsellor or by a clinical geneticist and there might be very little joint working at all so that the sort of sustained relationship with the family that the genetic counsellor can provide maybe isn't being provided for quite a lot of people. And so genetic counsellors might see

people with fairly discreet, defined conditions where the diagnoses are known and the counselling is relatively straightforward, and medics won't see them. And the more complicated diagnostic questions in those circumstances might not get the benefit of the counsellor support because they're completely separate, parallel working. I think that's a shame; I think a lot of that is probably driven by resource constraints and you know the number of referrals is clearly enormously greater than it used to be and there has not been an equivalent increase in personnel. So some of this is imposed by circumstances but I think it's been welcomed by some genetic counsellors and by some clinical geneticists who prefer that parallel working. I feel it's, I think that's a shame.

PH Can I ask, I mean in the training of clinical geneticists now, has there managed to be introduced a much greater component of counselling and related things, which there used to be completely absent until fairly recently?

AC Well there's certainly some of that and the trainees here will video record some of their sessions and then have an opportunity to go back over the videos with a supervisor so it's, well, the personnel have just changed but I think Anna Brazier I think will be doing that with them now. So that's very positive to have an experienced psychology or counselling type supervisor attending to those aspects of the consultation with them. And that clearly wasn't there before so that has to be good.

PH I remember myself how much I learnt from the sessions with Christine Evans and how a lot of the things one was doing intuitively one never realised until it was explained but they had a proper theoretical basis to them which you…

AC And she actually produced that lovely book.

PH Is there much interaction between the genetic counsellor scene in this country and in America? Because I've been very struck that, it's since the time I worked in America when genetic counsellors became a sort of independent discipline, but I was quite worried reading some of the things including the book by Stern that there seems to have been a kind of, not exactly confrontational but a pretty polarised situation that in America genetic counselling was something almost defined as being done by genetic counsellors and almost excluding clinical geneticists from the whole process. And that's been so different from the impression I've had as how things have evolved here. I just wonder whether there's been any kind of interchange or…?

AC Well the American board, or the genetic counsellor system, doesn't welcome people who have trained elsewhere so to work in the States as a genetic counsellor; they'd have to take the American Board exams. So it's a bit like in the medical system, I suppose.

PH Any reason for that?

AC I don't really see it. I mean I don't, I think it's very difficult to imagine that say the Manchester course or our course is so much inferior to theirs that our graduates wouldn't fit in. I think there's quite a bit of movement and cross recognition with other countries like Australia and Canada and European countries and so on, so I think it's pretty well the USA and the rest of the world, but I think it's being worked on. I'm not involved in it but talking to some genetic counsellor people at the AGNC, and they are negotiating with the Americans to try and get cross-recognition. So it might come.

PH Angus, just to wind things up a bit, I've been asking everybody I see two questions and the first of those is whether there's been anybody in particular that stands out as being important and formative for your career and general life in medical genetics?

AC Well I suppose I'd have to say yourself and John Burn. I mean clearly because both of you gave me my first two jobs in medical genetics and you know I've learnt hugely from spending time with you in clinic and in meetings and in general discussions. And that would apply to both you, you know. I also learnt negatively, I don't know if you want to use this bit but I'm quite happy to say it. When I started here you encouraged me to sit with everybody and I did. And perhaps it's had quite an effect on the

direction I took as well. I can remember being absolutely horrified by some of what I saw in just the one or two clinics which is all I could stomach of sitting in with a former colleague in Cardiff, and I found it really very difficult and that, so I had both a positive and negative role model to form myself around, you know. In some ways the negative, you know this is so bad that in some ways that was so clear and strong it was probably as effective as any positive image that I had.

PH [laughs]

AC Anyway [laughs]…

PH I don't think you'd recommend that for other people…

AC No, I wouldn't. No but it certainly was quite formative.

PH And then the other thing I've been asking everybody which may be quite tricky because you've been involved in a lot of different areas. But if you had to choose just one contribution that you've made that you'd like to sort of hang onto, not necessarily that's the most important scientifically but the one that you feel has been particular for yourself. Does anything stand out? I should say a lot of people have asked me to be able to have two and that's fine.

AC Oh, that's difficult. I'm one of these people who sort of I suppose has done, is doing, quite a few different things. I do get the strong sense that I should be focussed and seriously committed to one thing and excellence in that you know that's the strong message that one is given these days. And I don't fit into that at all; I probably have far too many fingers in different pies and never do any of them well enough. So it's very difficult to put…

PH Well I can plead guilty to that myself.

AC Well yes, well maybe you've had fingers in many pies but been very successful at all of them. To be honest I'd rather answer that in a year or two, because if we manage to get, if I manage to make a contribution to the ectodermal dysplasia treatment trials that are just beginning over the next couple, the next few years, then I think it would have to be ectodermal dysplasia; seeing it through from the mid-80s to treatment now. If that doesn't work out for whatever reasons in terms of the governance issues and the practicalities, so if that doesn't work out then it would be harder to make a choice because it would be some social science stuff, I'd want to be flagging up also some of the Rett syndrome work you know. But I think if I can say that I've been around from the linkage studies through to the treatment and also had a social science component in there too then I would probably pick the ectodermal. But maybe I need to hold my judgement a little bit to see how that works.

PH Well Angus we've talked about a good few things and I think I'll draw it to a close there. But is there anything that you feel is really important that we've not gone over that you want to bring up?

AC I think you've asked me about each of the areas that I've attended to over the time. I don't think so, Peter, I think you've…

PH Well thank you very much indeed, Angus.

AC I've enjoyed it, thank you. A chance to witness is always good.