John Hamerton

Personal Details

Name	John Hamerton
Dates	1930 - 2006
Place of Birth	UK (Brighton)
Main work places	Harwell, London, Winnipeg
Principal field of work	Human cytogenetics, prenatal diagnosis, gene mapping
Short biography	See below

Interview

Recorded interview made	Yes
Interviewer	Peter Harper
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Personal Scientific Records

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

Biography

John Hamerton was born in Brighton, UK, and studied zoology at Imperial College, London. In 1951 he joined Charles Ford at the Harwell Medical Research Council unit, working primarily on radiation effects on mouse chromosomes, but in 1956, with Ford, confirmed the correct human chromosome number as 46. In 1959 he moved to Paul Polani's unit at Guys Hospital, London where he was responsible for the discovery of the translocation of Downs syndrome. In 1969 he was appointed head of Human Genetics at University of Manitoba, Winnipeg, developing prenatal diagnosis and also involved with human gene mapping.

INTERVIEW WITH DR JOHN HAMERTON, 26th OCTOBER, 2004

PSH. It's Tuesday 26 October 2004 and I am talking with Dr John Hamerton at the American Society of Human Genetics Meeting, Toronto, Canada. What I have been doing with these talks is starting at the beginning. Can I ask you whereabouts were you born and brought up?

JH. I was born in Brighton, brought up, initially in Hove I guess, on the south coast, and then the outskirts of London, Wimbledon, throughout the war; I went to prep school at Haywards Heath, which was evacuated to Herefordshire during the war and then to King's College Wimbledon, my public school, and then onto Imperial College where I studied zoology.

PSH. Was there anything in your family background that took you towards science?

JH. Absolutely nothing. Nothing whatsoever. My father was a classical scholar, he taught, he taught in Nigeria for a time and then actually worked for, when he decided Nigeria wasn't the place to take a wife or bring up a child in those days, it was called the white man's grave I guess in those days, he came to England and worked for the rest of his life for Dr Barnardo's homes as a fund raiser and ended up as Deputy Director I think. My uncle was also a classical scholar, taught prep school in Scarborough. My grandfather on my father's side was a parson so I have absolutely no scientific background whatsoever.

PSH. I mean . . .?

MH. What got me into science?

PSH. Yes.

JH. Well I left school, I guess in about '45/ '46 just when everyone was coming back from war. I actually wanted to do medicine and got accepted I think, certainly at the London Hospital, I may have got accepted at Kings as well. Can't remember that, but got accepted at the London, but the proviso was I went and did my military service first and I decided I didn't want to do military service so I went to Imperial College and did the next best thing which I thought was zoology at that time. What got me into genetics was a summer job actually. I was interested in genetics, I became interested, I'm not sure why, I can't remember why because the specialities in Imperial College at those days, entomology and just at the end parasitology were the two specialities; I did entomology and the most likely place I would have ended up from Imperial College was the Colonial Civil Service chasing locusts around Africa. I didn't particularly want to do that. So what in fact happened was, I applied to, I got interested somehow in chromosomes. I applied to Pio Koller initially to work at the Chester Beatty for a summer job and he rejected me basically on the grounds of my eyes. He said I couldn't look down a microscope, I would never survive looking down a microscope. Today that would be discrimination but then in those days that was a reason for rejecting somebody.

PSH. Why did he think you couldn't look down a microscope?

JH. I don't know. I have no idea. Anyway Pio and I were good friends after that. Anyway I said, to hell with that so I went to Harley Street and had my eyes checked out and the guy told me off. Why did you wear glasses and there was no reason why you should. So then I got a job actually, a summer job with Janaki Amal, who was one of Darlington's students

PSH. In Oxford?

JH. No, at the Wisley Royal Horticultural Society gardens at Wisley. I spent my summers doing plant crossing. I am not particularly interested in botany. I mean botany is something we studied but I have always been more interested in animals than plants but I got the job there and I spent two summers at Wisley; at the end of the last summer, she was a student of Darlington who was still at the John Innes in Merton at the time and I spent, I think it was probably maybe the last month of the summer in Darlington's lab with Muldal, who was interested in earthworms and studying the chromosomes of earthworms. That's how I got interested in animal chromosomes.

PSH. I have always associated Darlington exclusively with plant chromosomes.

JH. No, he and Muldal, well Darlington did, Darlington and Haque did the study of Man, Darlington/La Cour, they all studied human chromosomes and counted 48. Muldal, he did work on, can't remember his interest, he worked on earthworms which had peculiar chromosomes. Anyway that got me interested in chromosomes. I did my undergraduate thesis, was sort of genetics. It was on phase change in locusts and in fact after I graduated I was accepted to go to Birmingham to work with Mather and Jamieson to do a PhD on genetics of phase change in locusts.

PSH. During your undergraduate time you were at Imperial, but there were all these geneticists, people like Haldane and Penrose and people up at the other end of town so to speak. Did you have contact with them?

JH. Not then no, not really.

PSH. So Imperial really was like being at a separate university.

JH. We were major rivals with University College. I mean University College and Imperial College were *the* rivals I think. And Imperial College to some degree considered itself to be a separate university. It gave its own diploma, its own associateship, I still have an ARCS Associateship to the Royal College of Science which you get automatically with your Batchelor's degree.

PSH. So you can't really, or it isn't fair to say those people influenced you at that particular time?

JH. Not in the least bit. No. What happened was that I foolishly also got married immediately after I graduated, my wife became pregnant with twins and

PSH. You needed to support yourself.

JH. Well I didn't know that at the time. We didn't have prenatal diagnosis in those days so I didn't know she had twins. My undergraduate stipend of I think it was £350 a year didn't seem to be adequate and then what happened. You see it was the issue then of military service as well.

PSH. You had had it deferred.

JH. I'd had it deferred and quite frankly I wanted to keep it deferred. Doing graduate work was one way of maintaining deferment. But there was another way of maintaining deferment and that was to work in Government Service and Charles Ford was, I guess I saw an advertisement, I can't really remember. But anyway Charles Ford advertised for somebody to work with him at Harwell and I had already been accepted to go to Birmingham and I decided the salary there was £415 per year which was a little better than £350.

PSH. That was for a PhD?

JH. No, that was not for a PhD. In those days a PhD was less important than it is today. Essentially I went there as a graduate student, you know you went there as what was the classification, MRC Grade 4, or something like that, scientist you know.

PSH. That was Harwell?

JH. That was Harwell and I went, I remember, for an interview with Charles and somehow he accepted me. I had not really done any cytogenetics. I had had that little bit of experience from Muldal, but he accepted me. I then had to tell Mather that I wasn't going there. Mather didn't speak to me for probably the next 5 years as it took him another year and it would have been a non-project anyway you know.

PSH. Was that very much in mathematical and quantitative genetics?

JH. It would have been that type of thing I think and with Jamieson who was one of his co-workers there.

PSH. What year are we at now?

JH. I graduated, I went to Imperial, we're at '51.

PSH. So that was the year you went to Harwell?

JH. Yes, I went to Harwell but in fact, what I did then, Charles wanted me to get some training so I in fact went to Edinburgh then. I went to Waddington's shop in Edinburgh and worked with the Slyzinskis.

PSH. They have cropped up several times.

JH. Slyzynski and Slyzynska, a man and wife who were doing chromosome work, mammalian chromosome work and frankly, I think probably I would say I learned less than nothing, very little there.

PSH. I was told they might still be living in Edinburgh. That's what I . . .

JH. They can't be. Well they must be over one hundred if they are living.

PSH. Am I right, were they some of the people who came over for the Edinburgh Congress I was told . . .

JH. Yes I think so.

PSH. and they couldn't get back because war broke out.

JH. That's right, they came over for that, that's right, so anyway, they had the animal genetics unit there. I of course met Waddington and I met Toby Carter, Mary Lyon, Rita Phillips, who were all there at that time before they went to Harwell.

PSH. That was something else I learned, that the unit up there in Edinburgh moved en bloc down to Harwell.

JH. Moved en bloc down to Harwell, later I think but I'm not sure whether it was until we moved to the new building, because we were in the old buildings at Harwell initially. I was up there until January/February from September/October until January/February and my wife was down there and she delivered in January and I said I wanted to be down there.

PSH. That was about 1950.

JH. My children were born in '52.

PSH. '52.

JH. So the Autumn of '51 I was in Edinburgh and that is where I learnt a little bit about mammalian chromosomes, but basically I learnt all I know, or knew at that time from Charles Ford, who was actually not working on mammalian chromosomes at all. Charles was working on Vicia fava, the broad bean, with root tips.

PSH. Was that really to study the radiation.

JH. Yes and I was, you've sort of taken me back, I was hired really to transfer some of the work Charles was doing on radiation work on plants to animals and the model we chose was the newt Plurodeles which was a newt which, and the idea was to use the larvae, the tail tips of the larvae which you could cut off and make preparations while they regrow more tail tips and so on. And that's how I came to know and meet Haldane. Actually I didn't want to meet Haldane, I wanted to meet Spurway. At least I thought I did.

PSH. Yes. She seems to have been a pretty formidable character.

JH. It was an interesting morning. My first paper actually is in the UFAW handbook on how to raise this wretched newt. The first paper I ever wrote. I was sort of registered for a PhD at the time as well, London University external PhD where Charles was my supervisor, and so I went back to Harwell and started working down there and then we needed these newts and Helen Spurway was one of the few people who had a colony of these things, so Charles arranged for me to go up to University College to meet Helen Spurway, at a certain time, half past 10 or 11 o'clock in the morning. So I arrived at University College, young graduate student not having the faintest idea what the hell I was doing, and arrived at the zoology Department at Helen Spurway's office, somebody said it's in there you know, so I go in there and I sit down. Nobody's there. Sit there for half an hour wondering what the hell to do, the door opens and a grizzled old head pokes around the door [grunts] "who are you?". I said I am waiting for Dr Spurway, so "[grunt] guess she's still in bed. I'll go and get her". Eventually she turns up, we do our business and she takes me to lunch at that pub across the road from the University College, it's no longer there I think on Euston Road where she used to go to have some lunch and then takes me back to the staff common room for coffee with Haldane and some of his students. I'm working for the government. Haldane is still at that point communist, 4 years turned and it was really quite frightening in a way, you know, in the sense that I was harangued how could I sign the Official Secrets Act, which I had done of course when I was working at Harwell, it was very wrong, it was just the haranguing. Anyway that's my story about J.B.S. Haldane. Subsequently I went on one of his courses I think statistical genetics which I totally didn't understand one little bit. He was the worst lecturer I think I had ever attended a lecture on. That was later on too.

PSH. What about Charles Ford?

JH. What about Charles?

PSH. You worked for him or with him for 7 or 8 years? Is that right?

JH. I worked with him from '52 to '56.

PSH. I see. I met him one or two times, I never knew him, but again hearing from others he seems to have been really quite a character and a half in his way?

JH. Charles was a great guy. Charles was a character, but he was a great guy. What I think I liked about Charles was he allowed you to, and there were certain things we had to do. We spent a lot of time working on mouse translocations and the cytogenetics of the radiation mouse translocations and that was sort of the prime thing we were doing you know, looking for marker chromosomes. One of the things we were interested in obviously was radiation protection. Next door was John Loutitt and David Barnes, who were doing bone marrow transplants and things like that and one of the things we were looking for in these mouse translocations was marker chromosomes, and eventually found the T6 chromosome which we used as a marker to settle the question as to whether bone marrow transplantation was actually repopulation of the bone marrow with foreign cells, i.e. the development of chimeras or was it a humoral effect leading to some form of chemical protection, because quite clearly they knew it was leading to protection but they didn't know why. And we actually got the group - Loutitt, Barnes, myself and Ford, got the Robert Rose de Villiers Prize from the Leukaemia Society of America for that work which was published in Nature in 1955 or '56, that was really the first, I had totally forgotten until today, that was the first demonstration of actual repopulation of bone marrow cells by foreign cells after radiation, the basis of bone marrow transplantation today.

PSH Absolutely.

JH. So that was one of the things we were doing, but because we were doing that we were also interested in developing cytogenetic techniques, I mean that was bone marrow somatic cell chromosomes. I mean one of the things we were doing was trying to develop techniques that allowed us to count chromosomes reliably and to recognise chromosomes.

PSH. Am I right, this was all on the mouse?

JH. This was all on the mouse until we also then, for some reason, I have no idea why, oh I know why, exactly why, it's all sort of coming back to me. We were also looking for a better mammalian model, OK. So we started looking at a variety of different species to see whether we could find a mammal which had a lower chromosome number, larger chromosomes that we could actually do things with, and one thought was marsupials, which we knew had lower chromosome numbers and Geoff Sharman came over from Australia and worked in the lab for a year, year and a half, something like that and developed a colony of marsupials there, but we also looked at other species, we got different species from the zoo and things like that, I think there's a paper somewhere way back on various different species we looked at, but we went out and trapped some animals around and we found the shrew.

PSH. Yes.

JH. Which when we looked at the chromosomes of the shrew, we found differing chromosome numbers but that was the nice thing about that. The nice thing about working for the MRC and John Loutitt as head is, it's nothing whatsoever to do with radiation, but we were allowed to go on and actually work out chromosome polymorphism in the shrew which is the first example again of polymorphism in an animal species.

PSH. This is a recurring theme in people I have talked to.

JH. And Tony Searle and his, not Tony but his son.

PSH. Yes he mentioned that, I forget his son's name but he told me that he had gone on.

JH. Working on the shrew.

PSH. It's is a fascinating

JH. Absolutely fascinating story.

PSH. And the MRC seem to have been flexible enough in those days to let people have their head, so to speak.

JH. Yes provided we did the work they wanted us to do, the radiation work you know, that was key. Charles, he was a great guy in a way. His main failing was he didn't like publishing. If you look at Charles's bibliography, very little published on his Vicia work, very little published in the early fifties and it wasn't really until we got on to the mammalian work that Charles began to publish and I guess I may have had some influence there, because to me, a young scientist,

PSH. You had to publish.

JH. I had to publish. What I didn't achieve there was my PhD, you know I didn't achieve my PhD. I never achieved a PhD and in the 50s and early 60s it didn't matter much and in the end I submitted my published work for a DSC, when it appeared I might want to come across the Atlantic, although again that was a fluke, but that dates back too to that period, why I came to North America, why I came when I did. Just going back, so we worked on the mouse, we worked on the shrew, we worked on a number of other species which we got, some from the zoo and other places you know and we didn't do anything on man basically.

PSH. So when did you?

JH. Well what happened I think, in the early fifties it was clear man had 48 chromosomes. It was there and I think in '55 we had a visit from a urologist from Oxford who was just visiting as people do you know, and he said to Charles I can get you some human material if you want. Charles said, sometime when we've got time we'll have human material. We had the techniques, we had the ability to look at meiotic chromosomes, which not many other labs did, not to the degree we had the techniques available and anyway Ursula Mittwoch had done a count and it had come out at 48.

PSH. That was Down's was it?

JH. Yes I'm not sure what it was, but yes she'd come up with something and it may well have been the correct count, and Hsu had looked at them and we had used his technique of his, what was once again a serendipitous observation, of the hypotonic solution to the spread of chromosomes which came from T C Hsu's lab in Texas and he got 48 and everybody seemed to get 48. Then we got this offer of human material and we sort of said, when we've got time we'll do that, we are very busy and we had all this other stuff going which was quite exciting, didn't seem there was a rush. And then on the grapevine, as these things happen you know, we heard something about Tjio and Levan's work before it was published and so Charles got back to the urologist and we very quickly got testicular material at the end of '55 and did the studies and confirmed Tjio and Levan's counts. But before that of course there had been the Melanders in Denmark [Sweden] who had not published because they could only find 46 chromosomes and they thought they were wrong and, you know, Tjio and Levan were working on cultured cells so they weren't convinced it was 46, I mean that would have been 48 in the textbook since 1921. Although if you read Painter's papers he wasn't sure either. It was only in the second paper where he actually comes down to 48. In his first paper he said the counts were 46 or 48.

PSH. And were your studies absolutely conclusive that it was 46?

JH. Yes we were. I mean we were looking at both spermatogonia and we looked at spermatocytes, and it was quite clear there were 23 bivalents there and that the X and Y occasionally didn't, you know, combine that with Tjio and Levan and it became quite clear that it was 46 chromosomes. So we published in Nature and the rest is history so to speak.

PSH. Did you look at bone marrow at all at that time or not?

JH. No. I then left. I still had ambitions to be a zoologist at that time and I had worked with Charles for 4 or 5 years and yes I was to some degree a bit ambitious. I needed to branch out and I thought I needed to move up a bit too, so I actually applied for a job with the Scientific Civil Service to work as a Scientific Officer, a Senior Scientific Officer at the Natural History Museum in South Kensington and the curator of zoology there at that time was Peter Pocroft, an Australian, and the thought was we could do some cytotaxonomy there and they were going to equip me a lab for doing cytotaxonomy and things like that. The only job I have ever walked into, the day I walked into it was the day I started looking for another job. But I still kept an interest in human chromosomes and continued to do some work because at that point Kodani from Japan came up with the thought that there was actually polymorphism in human chromosomes, 46, 47, 48 and was supporting the 47 count of De Winiwarter years before and that obviously had to be resolved, so I got in touch with the people at, I still worked with Charles, in touch with people at the urological hospital, St Phillip's or whatever it is in London, and was able to collect testicular material and go on working on that and quite a number of other counts just to confirm that it was not just in the Caucasian population 46. I have a fairly rigid memory of that because I was collecting testicular material the day my father collapsed and died and I was in an operating theatre from 8 o'clock in the morning until 6 o'clock at night and my mother couldn't get in touch with me and hadn't the faintest idea where I was.

PSH. Oh dear.

JH. So it is sort of riven in my memory a little bit. Anyway we did that and I guess my career sort of took its current path because I was interested in these things. I stayed at the BM from 1956 I guess until '59 and during that period I went to both the King's College, you know about the King's College meetings?

PSH. These were the first human chromosome meetings.

JH. Really yes. One was more sex chromatin, for which Murray Barr came over and where I met Murray Barr, Harold Klinger, people like that who I worked with subsequently. Murray came over, was a reason why I'm in North America, I met him then and both those meetings I gave a paper, first or second one on another mammalian species which had much larger chromosomes and you could look at the segregation of the X and Y, the question still then, one of the questions still unsettled at that point and in fact has only been settled in the last two years really is whether there is true crossing over between the X and the Y, and this species, East African species of rodent, has very large X & Y chromosome so you can at least have some idea of this and actually see some chiasma relation in there.

I talked about that at one of these meetings and the other person I also met there of course, who was key in my career was Paul Polani and Paul was just, now I have actually, what I could send you, is the thing I wrote for Paul's dinner because I gave a little bit of the historical thing,

PSH. That would be very nice indeed. That would be wonderful.

JH. on Paul 's career because that's interesting too how he got into this you know it's

PSH. I should appreciate that John very much.

JH. I think I've still got that on my computer.

PSH. So this must have been around 1958 or 9?

JH. This would have been '58/'59 I think, the first meeting was probably '57 which was primarily sex chromosomes. These were organised by two pathologists Davidson and Robertson-Smith at King's College and in those days virtually everyone who was in the field was at those meetings. It may have been 30 people there.

PSH. So were you actually working at Guy's in '59?

JH. No. I went from the British Museum, which I had to get out of, after 3 years I couldn't take it any longer, and I went and worked for a very short time with Danielli at King's. It's quite interesting. He was a man before his time too. He was interested in '59, if you can believe it, in targeting drugs to tumours.

PSH. That's amazing.

JH. And he thought that he could target drugs, you know direct them to the tumour so if you were doing chemotherapy you'd kill the tumour but you wouldn't do damage to other things.

PSH. Was that with antibodies or direct?

JH. I can't remember how he had to do it, because I wasn't particularly involved in the research. He wanted somebody to organise some trials and things like that. I was there and I went to a King's College meeting, anyhow I met Polani at King's College and I had just gone to Danielli's you know. He said I am looking for a cytogeneticist to do human cytogenetics. And I said, yes that's great. I would love to do it. But how are we going to do this, I have just started a job with Danielli. I had already screwed up my reputation with Mather, I didn't want to screw it up with anyone else. So he said well come and talk to me. I went and talked to him and we did something, a bit dishonest I guess. You write an advertisement fits your career, put it in the Times, I'll put it in the Times, then you can take it to Danielli and say "Look this is my dream job" so I did exactly that. The advertisement appeared and I went and saw Danielli who was a nice guy and I said "look this is the job I really want. I want to do human cytogenetics. I want to work in this area" He said 'go for it' and so I went for it, got the job at Guy's and again the rest is sort of history.

PSH. So that was 1960?

JH. That was 1960. February '60 I went to Guy's.

PSH. So Paul Polani would have already then been involved in his Turner syndrome work and

JH. Yes with sex chromatin primarily. They didn't have anyone able to do chromosomes at that point.

PSH. Except Charles Ford I suppose was involved?

JH. Charles, oh yes, Polani collaborated with Charles during that period. Polani and Charles collaborated and of course the other group was the Edinburgh group who were working there, and there were certain, I didn't really know the history, but Jacobs of course went also, Jacobs and Harnden. Harnden followed me as the next sort of young guy who went to work with Charles, primarily to develop skin cultures and because clearly if you are going to do massive studies on human beings it has got to be on a tissue, despite the lack of ethical permission and all the rest of it in those days. I mean 90% of what we did in those days you probably couldn't do today. No ethics review board would accept it and we'd never get consent. The guys we took testicular material from had no idea, they were having surgery for something else. Completely different, I can't remember why but they were having construction or something. They were operating in the testicular area and the surgeon said would you be able to test this.

PSH. In many ways it's reasonable.

JH But you couldn't do it today

PSH. You couldn't, no.

JH. Jacobs actually went to work with Court Brown, she again was a zoologist I think. She I think trained with Callan at St Andrews and then the two groups were Ford, well I mean the three groups were Guys I guess, Penrose and Court Brown in Edinburgh and a little bit I guess, beginning a little later probably, was Stevenson in Oxford with Fraccaro and Lindsten. Fraccaro then went to work for some time with Penrose at the Galton.

PSH. One of the things which Paul Polani said to me was that it was quite difficult to persuade Charles Ford to work on humans, that his heart really was much more in the mouse and the mammalian work rather than the human work. Is that reasonable do you think?

JH. I don't know. I had sort of lost direction, I mean I still kept in touch with Charles in the 56-60 period but Charles certainly was interested in the mouse model. I think as a scientist he thought more could be got out of the model than out of just counting chromosomes in humans you know. Penrose of course was interested in Mongolism or Down's syndrome, as it is now known, and there was a certain amount of rivalry between the groups, and Court Brown sent Jacobs, as I understand it, to Ford for training you know basically and a certain degree of, which lasted for a bit, now what is the word, feeling that priority had been sort of taken away and that the Jacobs and Strong paper potentially should have Ford on that as well. So I'm not sure what happened there, but they certainly weren't friends, the Edinburgh group and Ford certainly weren't friends for a considerable period of time.

PSH. When you got to Guy's what was your remit there? Was it to develop human cytogenetics?

JH. Yes.

PSH. Really? Generally?

JH. Yes. Yes. Polani was a very forward thinking physician actually and he had the remit from the Spastics Society to solve spasticity and he felt he needed genetics to do it. I mean it was one of the first, with the possible exception of Penrose and Carter at Great Ormond Street and John . .

PSH. Fraser Roberts?

JKH. Fraser Roberts, who also ended up at Guy's, those were the three groups doing genetics in London. Yes my remit was to do human cytogenetics and to set up a cytogenetics lab and I went there as a lecturer and subsequently senior lecturer in human cytogenetics at Guy's. That was exactly my remit, to set up the lab and do it.

PSH. And what was the first main project that you took on?

JH. Down's syndrome. Down's syndrome with Cedric Carter and I mean we, Guy's and Great Ormond Street collaborated and we did not collaborate with Penrose, you know, there was a break there.

PSH. That's interesting because I saw that a number of your first papers in that time were involving Cedric.

JH. Yes, well Cedric had the Down's and young Down's and we were interested in, I mean I was interested in translocations and so one of the first things we looked at was a series of Down's syndrome patients' families and were able to demonstrate inheritance of Down's syndrome through translocation

PSH. Yes. But am I right that even at that stage, Penrose was not really set up properly for cytogenetics?

JH. I can't really answer that. He had Fraccaro there and the people who went to the Galton I think were Miller, Fraccaro, Lindsten, they were both at the Galton for a time before they went to Oxford.

PSH. But my understanding is that there was nobody skilled like yourself at Guy's.

JH. No. Ursula Mittwoch was the nearest

PSH. I have spoken with Ursula and she freely admits she wasn't given the remit or resources to set up a proper lab.

JH. Penrose was, I mean my understanding, I was never a graduate student with Penrose but I am told by people who were that you sort of went there, you saw him once, you were given a problem and you never saw him again till virtually the end of your problem. And he of course was in Canada during the war, was in London [Ontario] during the war.

PSH. So coming back to Guy's at what point did the cytogenetics work start becoming a diagnostic service as well as a research area?

JH. I would say in the late sixties. I think it was a diagnostic service for certain things that we were interested in for research right through; Down's syndrome, Turner's syndrome, Klinefelter's syndrome. We did quite a bit of work on chromosomes in one or two surveys of the mental retardation population things like that, but certainly as an official NHS service it was much later, in fact it was towards the end of my time at Guy's. Like so many other things, the service was done, but as part of . . .

PSH. On the back of research.

JH. On the back of research, as it was here when I came here.

PSH. So it must have been a very, from everybody I have spoken to says it was an exciting time, those first years of human cytogenetics?

JH. Oh fascinating. I mean you found something new every day virtually. You never knew when you were going to find something new. The next guy who came to Guy's to work with me was Francesco Giannelli. He came in '60, soon after I did, as a student to learn cytogenetics and go back to Italy, and stayed here. Of course there has always been a big Italian connection with Polani, because Matteo Adinolfi and the other person who came to Guys, Georgiana Jagiello and Paul was a good director in a sense. He allowed you to get on with things. I think sometimes that, I don't know, my philosophy has been that when you take on an administrative job you sometimes have to give up some of the other things you do and he wanted to continue with his research, which I'm not sure his work on females, meiosis in the female ever came to very much you know. But it was certainly an exciting period and we had the resources, we didn't have to worry. You know in those days we didn't have to worry about grants and I'm sure I was infuriating because I wanted to go off and do things that I was interested in. I also did the human work that I was supposed to do but I went and did a lot of primate work with Harold Klinger. I was able to do that from Guy's.

I was interested in translocations, and segregation of translocations so we did quite a lot of that and that's how I sort of got to know Court Brown and Jacobs much more and the various, Court Brown in fact was one of my examiners for my DSC and I got to know him quite well in the end, because the differences I think between the Edinburgh group and the rest of us disappeared. Some of the chromosome meetings Jacobs organised, the chromosome meeting in Edinburgh, no, one other one, the Oxford chromosome conferences were important, although there were several sets of meetings in that period. The Basel meetings that Harold Klinger organised were very important I think in terms of developing interactions between different people and out of that came work I did, but you couldn't get any material out of London Zoo. It was so difficult to get material out of London Zoo but you could go to Basel and get primate material, you know, they were willing to anaesthetise their animals, if only lightly, and there's a nice story about that if you ever talk to Harold Klinger, ask him about the Orang Utan who woke up in the middle of the sample. He tells the story of being in the cage with this bloody great Orang Utan. I was outside the cage I'm telling you, and it was being put out, but fairly lightly, with one of these drugs and he was sort of sitting in the cage taking a blood sample or skin sample and he felt the hand moving up his leg. He got out of the cage fairly fast.

PSH. So what point was it that you started thinking of coming over to Canada.

JH. Well, a bit more than that actually. A couple of other things that we did in the interim. Giannelli of course got interested in X inactivation and

PSH. You were involved quite a lot too.

JH. I was involved in that, in fact I somehow got to work, again I can't totally remember how the interaction began, but with Roger Short in Cambridge. There were two areas we were interested in. Because we were interested in X inactivation and we wanted an animal that we could recognise the X chromosomes and fairly closely related animal and the mule and the hinny became . . . so that was . . . I was working with Roger Short initially on, again I cannot remember how these things started, but the extensive work in intersexuality. I suspect Roger called up or something and said I want to do some chromosomes, can you do it and we sort of agreed. Intersexuality in the goat, and then we decided to look at chromosomes of the mule and we needed the two crosses, so we went to Portugal to get the two crosses, that was funded by British Council and that was a fun trip too. One I'm not sure I ever thought I would come back out alive, having driven down some of the narrow lanes in the Algarve with the local government veterinary officer to collect . . . So we actually went to, and I vividly remember it. We went to one of the big slaughter-houses in Lisbon but you couldn't recognise, the sort of mules and hinny you know.

PSH. Were they breeding hinnies regularly as well as mules? I didn't realise . . .

JH. Yes and what we had to do was get to the village, and the local veterinarian had got the local guys to bring in the foals along with the parents, so that you could determine which was which because, I mean just looking at them there ain't that much difference. So anyway that allowed us to do the work on the X inactivation and that actually proved Mary Lyon was right and Grüneberg was wrong and one of my pleasanter moments was when Grüneberg got up on stage at one of the Genetics Society meetings and said "I'm wrong".

PSH. That was at least decent that he did that.

JH. Yes, that was after I'd given a paper and demonstrated this. Anyway how did I come to Canada, why did I come to Canada. I think it probably dates back almost to my meeting with Murray Barr. I came over to North America to work a bit with Margery Shaw at Ann Arbor, when Jim Neel was head there and do some work, I forget why I came over, it was at the time of the Chicago Conference on nomenclature, which I organised along with others, but the Chicago and that and somehow I got involved and went to work, maybe because of cell culture or something like that, somatic cell genetics, I went over to work with Margery Shaw at Ann Arbor for a month. And while there we went up to the Great Lakes Chromosome Conference, which was at that time held at London, Ontario where Murray Barr was Head of Anatomy and Fred Sergovich was doing cytogenetics. So I met Murray Barr there again, having met him previously and I guess I gave a paper there, I don't know, I can't remember, but anyway that was sort of my first trip. No it wasn't my first trip to Canada. It was my second trip to Canada. My first trip to Canada was the International Congress of Zoology in '58 in Montreal.

PSH. Was that the one where Lejeune actually gave his presentation on Down's?

JH. That's right. I went over to that and actually got stuck in Montreal for about a week because the plane broke down and in those days they didn't have another plane and anyway, so that was my first exposure to French Canada. I guess at the end of the sixties, again I had been nine years at Guy's, at that point I had applied for a number of chairs in Britain. I was a senior lecturer. I decided the British system was pretty hierarchical. I had my doctorate and the British system in those days was so pyramidal. One chair, he was there for life, if you wanted to be. I had applied for a number of chairs, all of which I had pretty well decided had been decided upon who was going to get it before the advertisement came out.

PSH. And am I right that cytogenetics really didn't figure much in the academic structure?

JH. Right, it didn't figure at all really. I forget what I applied for but I remember I applied for a number, decided I wasn't either in the right field or somewhere, and I got a letter from, oh I don't know; also in my personal life, I had had two divorces and I was married to my third wife and we at that point had one child and another one on the way and I thought it was probably time for a fresh start. Anyway a letter came from Harry Medovy. Two jobs actually, one Head of Anatomy at Queen's which I looked at at the same time.

PSH. That's Queen's here at Toronto?

JH. No in Kingston.

PSH. In Kingston, sorry

JH. Which was down the way down the lake and the other I had a letter from Harry Medovy, who was a paediatrician, Head of Paediatrics in Winnipeg and Murray Barr he was looking. Irene Uchida had just left Winnipeg to go to McMaster, and he was looking for a cytogeneticist to run the cytogenetics lab there, and the letter came in March I guess and I thought about it; I was recommended I guess to Harry. Harry had contacted Murray Barr to say do you have anyone in mind, he suggested me and I looked at the letter and thought for a minute and I said I will go and look at it anyway. My wife said "you can go and look at it but I'm not staying there more than 5 years."

PSH. This was 1970 was it or thereabouts?

JH. '69. March of '69 I had the first letter. Things got organised in those days quite quickly. I told Polani I had got the invitation and I think we were probably ready at that point. Ready to part company.

PSH. You wanted to run your own set-up.

JH. I wanted to run my own show and I didn't see how I was going to do it at Guy's with Polani and I didn't see that there was, I might have got a readership you know, but that was about it. I guess I was ambitious, young, brash, decided I wanted to make my own career. Anyway I came over and looked at it, liked what I saw. Looked at the job in Kingston, didn't particularly like what I saw. Got an offer of the job in June, came over and in those days they were very generous. I came over a second time, recruited David Cox, who was at that time working with Ted Puck in Colorado. Actually he may have gone back then, he did initial cytogenetics at the hospital for sick children and then went over to work in somatic genetics with Ted Puck and Arthur Robinson in Colorado and came back in July, started looking at houses, was offered the job, came over in September, got my landed immigrant status in about two months and had a medical exam at the thing and moved. Again that's not something you can do today.

PSH. Can I ask before we come on to your work in Canada, had you already started writing your book?

JH. Yes, I wrote my book, oh I guess I started it around ’64 or ’65. No ’65 probably. The first volume came out before I left England, second volume came out after I got to Canada.

PSH. Yes.

JH. Yes, in fact it was pretty well finished when I left England.

PSH. Then when you started in Winnipeg, one of the things I have noted from the papers was this longitudinal study of newborns. Was this something you started pretty soon after you moved here?

JH. Yes first grant I got.

PSH. How long did that go on for?

JH. Well we did 14,000 babies based on cord blood, I guess it went on from ’71 to about ’75. Again it was a study that could not be done today.

PSH. Absolutely not.

JH. We had no consent, nothing. We had all the names, we had all the information, we had all the demographic information, we had all the names. The only time we got consent was when we began to do follow-ups.

PSH. But that and its Edinburgh counterpart have really given a huge amount of valuable information.

JH. Then of course we started the follow-up meetings, there were about four or five follow-up meetings, one in Denver, one in Hawaii that Pat Jacobs organised when she was in Hawaii and one outside Winnipeg which we organised, at a resort outside Winnipeg; and those were valuable meetings too and we brought together all the - what’s unfortunate I think is we have never really followed those. We have done some follow-up but we’ve not done the sort of follow-up and we just can’t get the money for it now.

PSH. And yet it would be very interesting to know what has happened to these individuals in their 30s and 40s.

JH. It is very interesting you know. Last year out of the blue I had a call from a lady in Ottawa who was pregnant, she was of Chinese extraction, her father had never told her that we had detected a translocation and he didn’t want to know, never told her that and she had finally got some information out of him and she was pregnant. She wanted to know what her risks were. She got back and we still had all the data so we were able to get back to her and give her the data, give the people who were providing her with counselling today the appropriate information. We did quite a bit of follow-up actually, as long as we could and as long as we could get funding for it, but I would like to have seen it go on right through if possible, but it wasn’t possible. But I think roughly those studies, about sixty a total of somewhere in the order of sixty thousand newborn babies were studied in the early seventies in about five studies.

PSH. One of the themes which must have got going soon after you came to Canada was the whole area of prenatal diagnosis. You were really in on that more or less from the beginning weren't you?

JH. Yes Harry Medovy recognised that as a possibility and the other person who came to Winnipeg at the same time I did, because I'm not a clinician, so I said to Harry if we are going to run a genetic service we need a clinician and the person who came to Winnipeg at the same time as I did to become head of medicine at St Boniface Hospital which is one of the two teaching, was one of the two teaching hospitals in Winnipeg, was Bill McDairmid who had worked with Wintrobe, had been at the Galton for a time with Penrose, wasn't really a geneticist, was a clinician, he had actually started life as a General Practitioner in Saskatchewan, wanted to specialise in internal medicine, went to England to work at University College, came to Guy's, had met me I think but I had totally forgotten about it and was at the Galton for a time and at University College. I think he was over here for about a year and then went to Colorado to work with Wintrobe and was being recruited, it happened at exactly the same time I was being recruited, in the May of '69 and I remember there was one restaurant that everybody used to get taken to when you were being recruited back in those days. Now there are many you know. In those days there was one steak house that was good, and I went there to dinner and at the next table was Bill McDiarmid.

PSH. So he came as head of . . .?

JH. He came as head of medicine. We got him a cross appointment in paediatrics and he set up the clinical side of genetic counselling. In fact I came in September, we started a counselling clinic in December. Exactly when prenatal diagnosis started I don't know but we knew about it. We began probably to do it and then I got involved because at that point also the MRC under its Director at that time Malcolm Brown set up a genetics committee, so it was the first genetics committee, so grants and genetics began to get reviewed by a genetics committee which involved, I was on that, Jim Miller from Vancouver, Lou Siminovitch from here, Louis Dallaire and that group of four also then, I forget who else, oh Clarke Fraser

PSH. Clarke Fraser?

JH. Clarke, I forget who else but anyway, we started reviewing grants and genetics but also then prenatal diagnosis was coming in and Malcolm Brown wanted a study done or prenatal diagnosis and asked me if I was willing to, I don't know why he picked on me but anyway if I was willing to head up a cross country study on prenatal diagnosis, and a registry and things like that, so we wet up a working group which was Jim Miller and myself, Malcolm, Lou Siminovitch, Nancy Simpson from Queen's and Louis Dallaire from Montreal and that was the first sort of study and we did a registry of prenatal diagnosis and then, later on, I got involved in a cross country study comparing amniocentesis to CVS. The first things I was interested in, the other thing that was developing at that point, was gene mapping. The first gene mapping.

PSH. I was going to ask about that because, did you get into that through what you might call natural cytogenetic rearrangements, or was it through the cell hybrids?

JH. Through the cell hybrids.

PSH. Right.

JH. We started doing some work on cell hybrids. I recruited a post doc, Barry Richardson from Australia. He came over to do some biochemical genetics.

PSH Was Phyllis McAlpine already in Winnipeg at that stage.

JH. No. Phyllis followed Barry. Phyllis was again a Galton . . . Phyllis did her undergraduate work in London, came to Toronto to do a Masters with Peggy Thompson and then went to the Galton to do a, not with Penrose......

PSH. Harry Harris?

JH. Harry Harris and

PSH. Bette Robson?

JH. Bette Robson, to do a PhD, and then when Barry Richardson left to go back to Australia I was looking for somebody to do biochemical genetics and recruited Phyllis.

PSH. So that must have been a wonderful development, because with your cytogenetic expertise and her on the biochemical side.

JH. Yes, well Barry was also a biochemical geneticist beforehand and I'm not sure how I got to know him, but he was also biochemical and did some of the early work. Her work on enzymes and mapping sort of fitted in with what we were doing and was also able to do some other types of things, so she developed the biochemical genetics in Winnipeg and subsequently followed me as Department Head.

PSH. Can I ask, how did you get involved in chromosome 1 in particular in the early gene mapping meetings? Was it just that they kind of dished out chromosomes or was there a specific reason?

JH. Fluke! Well some of the markers that we had, Phyllis was particularly interested in certain markers; they turned out to be on chromosome 1, so we got interested in chromosome 1.

PSH. Because those early gene mappings were another kind of extraordinarily exciting phase.

JH. Yes that was again a fascinating period. I mean the first gene mapping meeting at Yale, the book is about 'that' size and it might have been 50 people there, organised by Frank Ruddle. I spent a little bit of time at Frank's lab at Yale working again with somatic cell genetics interested in the cell hybrids and had a PhD student who did some work on a Chinese hamster cell line which had been left there by one of the previous people. So we had a new Chinese hamster cell line and we were able to demonstrate segregation of chromosome sites [?]. But so much of, it all looks planned now, but a lot of it wasn't planned I tell you it was serendipity and you had something you did it and it turned out to be right.

PSH. That was I think the wonderful thing about those days.

JH. Yes and you could write a grant, you got funding for 3 or 4 years and now people are writing grants every day of the week. I got out of it. I held grants from the Medical Research Council from'70 through to '94 I guess, '93/94.

PSH. That was a good spell.

JH. I felt it was a good spell, and in '94 I began to realise I wasn't as competitive as I was and I got a terminal grant and I had already made the decision, in those days they gave you a terminal grant. They gave you a year, they gave you the same funding you had but just for one year. Nowadays you get cut right off.

PSH. Yes.

JH. And I made the decision, before I got the thing I made a conscious decision that if I got a terminal grant, I wasn't going to sweat at it, I didn't have to prove to anything to anybody. All I wanted to do was close my lab down in a dignified manner and make sure that people who were working with me were reasonably well-supported and were able to get other jobs and I did exactly that. I was able to get some local funding to back up my grant for a year and I had two post docs then, one of whom is now running a cytogenetics lab in Winnipeg and the other is running a molecular lab in Halifax, able to find them jobs and so I didn't have any real regrets.

PSH. John, we have gone over a lot of things, but are there any things which, any areas which you think are really important that I haven't asked anything about?

JH. I don't think so. I think the early period at Guy's was a very important period as far as I was concerned. It allowed me really to develop my own work and to develop some confidence in my own work, also allowed me to meet my current wife as it happens, who was a librarian at the paediatric research unit and should be credited with the fact that the index in my book is 100% correct and the bibliography in my book is 100% correct.

PSH. The two most difficult parts to write!

JH. Which she did almost entirely and was pregnant for a good part of the time while she was doing it.

PSH. One of the things I have been asking everybody I have seen is, in your career can you pinpoint one person who you feel has been a particular influence on how things developed, more than the rest of folk. It doesn't have to be one actually.

JH. In terms of mentoring I guess Polani in a sense. In terms of development of my career, I guess I would have to say it was Murray Barr, in the sense that my career really developed when I left, I mean in the sense of developing an independent career and doing what I did and the fact it was Murray Barr who basically made the recommendation to Harry Medovy who got, I mean I got the job but I wouldn't have been interviewed, wouldn't have been written to if it hadn't have been for Murray Barr, so it's Murray Barr in a sense. But I've collaborated with a lot of very good people, Roger Short who is now in Australia, an excellent scientist. Phyllis, great collaborator. Current, I mean people I have recruited. One of the satisfactions of a career I think, is seeing people you have recruited and recognised as having some talent, have gone on and done things. You probably know Jane Evans, dysmorphology. I recruited her as a post doc, in fact as a summer student in 1975 and her career went on as a National Health Scholar into dysmorphology, and Alisdair Hunter who's now in Ottawa.

PSH. The other thing I have been asking everybody is, if you had to choose one piece of work you feel kind of most proud of and you identify most closely with as your own, is there a particular piece or area of work you could pick out. Again I've allowed folk two.

JH. Oh I think it would probably be the Down's syndrome work we did in the early days. If I had to pick another, I think the collaborative work we did on some of the first clinical trials on prenatal diagnosis and where we really demonstrated the fact that not only drugs should be tested in collaborative randomised trials, but that other interventions should be tested in randomised clinical trials, and I think the CVS/ amniocentesis trial which was collaborative, I was chair of the Steering Committee but there were a lot of other people involved, but I think that was a landmark at the time. There were other trials going on but we were the first. Also the fact, Canada, surprisingly enough, was the first country to actually begin to certify and regulate the profession of medical genetics with the development of the Canadian College. I guess I have been fortunate enough since I came to Canada to be involved in virtually every development in the field. I was one of the founding members of the Canadian College and pleased to have some of those things recognised. I became a Fellow of the Royal Society here in '97, got the Order of Canada in 2002 so, the country's been good to me. I consider myself as much a Canadian now as I do a Brit.

PSH. Well John, thank you very much. I will close it there and turn off the machine but thank you.

(End of Recording)