Paul Polani

Personal Details

Name	Paul Polani
Dates	1914 - 2006
Place of Birth	Trieste
Main work places	London
Principal field of work	Human cytogenetics, medical genetics
Short biography	See below

Interview

Recorded interview made	Yes
Interviewer	Peter Harper
Date of Interview	12/11/2003
Edited transcript available	See below

Personal Scientific Records

Significant Record set exists	No
Records catalogued	
Permanent place of archive	
Summary of archive	

Biography

Paul Polani was born in Trieste and educated in biology and medicine at the universities of Siena and Pisa. He came to Britain in 1939 for postgraduate research, but he was interned when Italy entered the war in 1940, but was released to undertake medical work at Evelina Children's Hospital in London. After the war he developed research on congenital heart disease at Guy's Hospital, London, learning genetics with Lionel Penrose, leading to the recognition of Turner syndrome as a sex chromosome abnormality and of translocation Down's syndrome, in collaboration with first Charles Ford and then John Hamerton.

In 1960 he was appointed Professor and Director of the newly formed Paediatric Research Unit at Guy's Hospital which he developed as a broad institute for medical genetics research and services, with cytogenetics, biochemical and immunological genetics, epidemiology and clinical sections. This provided a major influence on the development of British medical genetics over the subsequent 30 years.

INTERVIEW WITH PROFESSOR PAUL POLANI, 12th NOVEMBER, 2003

PSH. May I start by saying it is the 12 November 2003 and I am at your home in Clandon [near Guildford]. It is very nice to see you and what I would rather like to do and, you interrupt at any point, is to start a little bit chronologically; start at the beginning and maybe use the material you sent me to inform some of the questions. So the first thing that intrigued me is, you were born in Trieste?

PEP. That's right, yes.

PSH. and my understanding is that Trieste kept changing hands and was part of various different empires. Did you feel, being born in Trieste, did you consider yourself Italian?

PEP. Oh yes, I mean I consider myself Italian because I come from an Italian speaking family. Although my father wasn't born in Trieste, nor in Italy. In fact my mother was born in Austria, technically speaking, because Trieste was Austria then. When I was born in 1914, Trieste was Austria, so strictly speaking I was an Austrian citizen. A citizen of the Austrian-/Hungarian Empire. And Italy obtained Trieste, as a settlement at the end of the first world war in 1918, and then automatically all those who were Austrian and residents of Trieste became Italian.

PSH. Yes

PEP. Or at least Italian citizens. So that is the story.

PSH. Do you think that being from Trieste made you perhaps, from the beginning, more international in your outlook than if you, say, you had been born in some other part of Italy?

PEP. Oh yes undoubtedly; well of course, Italy has an international history.

PSH. Of course.

PEP. All of it. Everywhere, anywhere but Italians were the rulers. But for a long time anyway. Let's say until 1960, if you want to go as far as that. Now however, yes I think in Trieste one was very much aware of the fact that you were part of a cosmopolitan group of people. There were people from the whole of the Austrian empire, whatever that meant. Therefore yes, Austrian, Hungarian clearly and people from Yugoslavia, as was then, and people from further south and of course there were lots of people there for business and trade because Trieste was the main inlet into Europe, in fact for a long time, not only Austria and Hungary but central Europe, even northern Europe, traffic went through Trieste.

PSH. Yes. I was interested in the notes you sent me and you said already at school you'd got interested in genetics. Do you think that your life in genetics was started off at that point, or really was it later that that came.

PEP. Well, perhaps I should say, that at least my parents, say, used to tell me I had always wanted to be a doctor of medicine, always wanted to do medicine. However, my genetics interest began when I was already at high school, so to speak. And they strengthened very much when I got to University, when I got to Siena. The first University I went to was Siena. I went to Siena which was a small university with very, very good teaching – 25 students per annum and so on, that sort of thing.

PSH. That's a wonderful thing to have, just 25 students.

PEP. It was wonderful really. Incredible. You had a one-to-one relationship with your teachers. And in the first year I really did essentially biology, which meant biology with a biologist; the professor of biology, D'Ancona, was a geneticist. He was a conventional geneticist of those days of course you know.

PSH. Yes

PEP. Peas and butterflies and various things of that sort and of course Drosophila We had a very good indoctrination into genetics with him and he was the man who saw very clearly that genetics would have an influence on human affairs, but particularly on medicine and through medicine particularly. So he was quite ahead of his time in that sense if you like.

PSH. Yes, because that was around 1930.

PEP. Yes, I started in 1932.

PSH. So he was ahead of his time

PEP. Yes ahead of his time. And his library, which was largely his own library in the biology department, was quite well supplied with genetic material. And I remember, I think I mentioned this, I remember Wilson for example.

PSH. That's his book "The Cell".

PEP. That's right, exactly. And that was you know, a 'mind-opener' of course among other things. But D'Ancona was very good. He was excellent and we had lots of practicals with him too. Practicals in the sense that we were able to look at Drosophila under a low power microscope and get a little bit of the hang of the biology of the organism.

PSH. Am I right that you moved across to Pisa for more clinical studies, or was it a sort of mixture of things?

PEP. No. No. I would have stayed in Siena but Pisa offered me the opportunity of getting into the Scuola Normale Superiore, which is a special institution in Italy, which was started in fact by Napoleon and which, where you are a student as an internal student, and then you are a student of the university, but you are internal of this Scuola Normale.

PSH. I see. That is something we don't really have at all in this country.

PEP. No, I think it is rather unique. Well I don't think there is one. No. Not as such and it was mainly for the physical sciences, but there was a group then in existence for medicine. And you entered this thing by competition. You had to sit an exam. And when I tried first I couldn't get in, there were no openings. So the third year there was one opening and I applied, and I had to re-do all my medical exams for the first 3 years. I mean the main ones, anatomy, physiology all that. And which was extremely good for me, but extremely painful at the time.

PSH. I am sure, yes. So would it have been be fair to say that people with that kind of studentship, there was an expectation that many of them would go on to do research.

PEP. Yes I think so. Fair enough. Yes. Either research or certainly.....

PSH. Something academic

PEP. Something academic. At least something academic.

PSH. The thing which then intrigues me, which you mentioned in your papers, was that when you finished there you seemed to have a fairly clear idea that you wanted already to study in England.

PEP. That's right

PSH. and am I right that this was something separate or additional to the problems of fascism and things in Italy?

PEP. Yes I think

PSH. Or was it all tied up?

PEP. Well you know, human affairs are always complex, and certainly fascism, which was something which I didn't like, was one thing. My father of course was himself a very clear democratic liberal man, and so we had this tradition as it were. Anyway that was one reason. The other reason was that, and this is a very funny story actually. When I was about - do you mind if I go back a little bit?

PSH. Fine. Fine.

PEP. to when I was about, let's say probably12, perhaps earlier, between 10, 11 or so perhaps, when I had what probably was a primary TB. At least I had an illness with loss of weight and cough and pyrexia. And in those days they kept me in bed for x months, 3 months I had to spend in bed. That was our GP. His orders, right?

PSH. Yes

PEP. Anyway during that time my mother, who wanted to keep me reasonably quiet, bought me the children's encyclopaedia, not in English, but an Italian translation. But it was entirely English.

PSH. I see.

PEP. I can remember the letter boxes for example, all that sort of stuff, the telephone booths and so on. And all the little Miss Muffett and all that sort of stuff, translated into Italian actually, but still with the dresses and things of the time. So I had this curiosity about England and about the history of England, and the third thing that was undoubtedly an influence, my desire to specialise in something. I didn't know exactly what, but the first thing I wanted to do was to get a good hang of international medicine, say British medicine. So I came to England also with a view of going to be a postgraduate. But when I arrived in England war broke out.

PSH. Yes, your timing, I mean you arrived in August 1939, which was just about the worst, well you could I suppose say maybe either the worst or the best time, but a critical time.

PEP. Yes I went to Guernsey for a month, for the first month, because I didn't know English of course. At least I did know a little bit of English which I had read in books and so on, but mainly technical, medical. And we had some very good friends who lived on the island and I stayed with them for a month and then I came over on the first of September, and then of course, war broke out and although I had digs just opposite Ducane Road, Hammersmith Hospital, there was nothing to do. It was closed.

PSH. So you went off as a ship's doctor.

PEP. Yes. Not immediately. That took a little time. Before that I had to make do. Life was not very easy because I had very little money, so one had to make do with whatever.

PSH. I liked your description of going around the Circle Line. I suppose a lot of people must have done that.

PEP. Oh I am sure so. Yes. You got warm. You were warm. You were comfortable. You were sitting. The other thing of course was that I immediately registered with the General Medical Council, because of reciprocity between Italy, Japan and UK.

PSH. So you had no problems in terms of your degree being accepted?

PEP. It was accepted, yes.

PSH. That was very fortunate.

PEP. That was very good. It was essential if you like.

PSH. Absolutely

PEP. So that happened and then I immediately registered with the British Medical Association of course, so I had the use of the library, which was essential, and so on and so forth. So I am a member of the British Medical Association since 1939.

PSH. I hadn't realised until reading what you sent me, of course, I'd known that there was quite a long time after there was war between Britain and Germany, when Italy was not directly involved.

PEP. Yes, it's about almost a year. 9 months, 9 plus months. Yes and during that time I was a ship's surgeon on a Naval Auxiliary in fact. It was a merchant man, but we had a gun, and we had a crew, a gun crew and we had a Commodore, right through the convoy area, this is to say right up to Gib.

PSH. I am interested that being Italian wasn't a problem in terms of being on a ship with sort of military things happening around.

PEP. No there was no problem. Because I think there were probably two or three reasons for that. First of all, that like most doctors I was assumed to be a non-combatant.

PSH. Yes

PEP. That was the first thing. Secondly, they knew I left Italy out of my own volition. Fascism wasn't my strong line shall we say. Thirdly probably, the fact that, yes, they needed doctors, because I mean we were short of doctors of course, immediately with everybody going into the armed forces, the younger men. So yes I was on this ship and it was quite an interesting time.

PSH. And then it seems more or less when you got back, then Italy came into the war.

PEP. Yes, as we were sailing back, Italy entered the war so I was really an enemy alien on board of this auxiliary vessel.

PSH. I was very interested that, well, perhaps the most important thing was that you weren't on the Arandora Star, I mean

PEP. Yes I missed it by good luck shall we say.

PSH. You see, I think most people now won't know what the Arandora Star is or was, but perhaps the only reason I know is because South Wales has a very large Italian community. There were a huge number of people who had lived in South Wales for many many years, who also were declared enemy aliens and then put on the ship and of course died. And this is still remembered in South Wales as a terrible catastrophe

PEP. Really?

PSH. because it's a very close community and it is you know, so the fact that you were not on it, if you had been on it things might not have gone any further, might they?

PEP. Indeed. I had one or two friends who were there. One of them died and two or three of them saved their lives. One of them was Professor Limentani who then became Professor of Italian at Cambridge.

PSH. Really.

PEP. Later on. He was a very good literary man.

PSH. Yes. So you stayed in the Isle of Man.

PEP. I Stayed in the Isle of Man.

PSH. A lot of other eminent people too

PEP. Quite a few people yes. All sorts. I had a sinecure actually. I had the hospital, so to speak.

PSH. One of things that always amazes me is that there are a series of people who came to Britain, essentially often seeking refuge or very worthy pursuits and then were herded up and treated in really a pretty terrible way. And the thing that amazes me is that on the whole, at least those people I know and have read, seem not to have been bitter about it.

PEP. Well I think there were a lot of reasons why internment then was almost a necessity. First of all there was the risk of invasion by the Germans

PSH. Yes, which was very real.

PEP. Which was very real. Secondly, there was the beginning of what one called then, the 5th column and all that that implied. Thirdly, undoubtedly there was the fact that the foreigners themselves were at risk of being misunderstood or mishandled almost, if you like, by people who didn't know about them.

PSH. I hadn't thought of that.

PEP. and how would you segregate the good from the bad and how would you deal with people whose language was obviously foreign and whose appearance is often very foreign, and so and so forth. So I think you could

say that both for the benefit of the population, the British population, but also for the benefit of the internees, the future internees, that was a very sound policy. Besides that, internment was not anywhere a terrible thing. I mean, yes you were not free to move about. Yes you were behind barbed wire. Yes you were housed in conditions which weren't exactly your own bedroom, you know, and all that sort of thing, but really we were very well off.

PSH. Yes. I have read Max Perutz's account of being an enemy alien and there must be many dozens of people who have made big contributions in Britain in their later lives, who went through all of this.

PEP. Yes obviously. There is, I think I quote a book by this chap, the Island of Barbed Wire

PSH. Yes, I must try to find it.

PEP. I've got a copy here if you would like to borrow it. Anyway.

PSH. So then after the Isle of Man you then got seconded down to the Evelina

PEP. Yes. Well actually it's a round about way. I don't know whether you want me to expand on this.

PSH. Yes, do.

PEP. I had volunteered for the Pioneers and they told me, "no don't worry about the Pioneers. You go and do your doctoring in London, which will be more useful". So I registered then with the emergency medical service during the war and the man who was running it from the medical side was Dick Bonham-Carter, whom I didn't know of course then. I met him. And he was organising for me a job with Professor de Wesse Low [?] to do blood pressure work, which was wanted for reasons of war casualties and so on. And luckily a person whom I knew, who was at Evelina, developed measles and that person was the only medical officer in the Evelina. And they said, would you step in for a couple of weeks while you are waiting for this job with de Wesse Low. I said "with pleasure. I don't know very much about babies but I will try or let them try me", and I stayed for 8 years. Because then the resident didn't come back. And I was there for many years really, from 1941, that's right early 41, until '48: but till '45 or '46, no '47 I was the only resident you see.

PSH. That's amazing.

PEP. Which was very excellent for me.

PSH. I hadn't realised that as well as all the medicine you have had to do the surgery.

PEP. Yes I did . Well it was mostly emergency surgery but also some non-emergency surgery, for example, ENT surgery you know, tonsils and adenoids and that sort of stuff.

PSH. They wouldn't let people like us do that now.

PEP. Oh honestly. What we did then, really, it's just incredible. You wouldn't be able to do that. You wouldn't dare do it.

PSH. No. No.

PEP. In addition to that, at the Evelina hospital there was a first-aid post and I was in charge of that, and that wasn't exactly a light duty, because we had casualties quite a lot. I mean not serious casualties, but flying glass and splinters and broken legs and that sort of thing.

PSH. Was the Evelina linked at that stage with Guys already?

PEP. No, not as such. The link became, came on very quickly however, because the Evelina did not have any pathology services to start with, so we started by having the major pathology done by Guys, although the sort of home pathology like blood tests and urine and so on we did ourselves of course. And we did our own X-rays. We had a Canadian Red Cross portable machine. So you know, but really I think we came under the aegis of Guys around '42, I think, already. And then about '43 I think, we started getting students in from Guys because paediatrics had been closed at Guys, had been evacuated to Kent somewhere, and so students missed the paediatrics and they came to us. So I had a bunch of these students, so much so that at that moment they declared me a recognised teacher at the university.

PSH. Good

PEP. Yes it was great fun and the students were extremely good and helpful and there were multiple pairs of hands, extremely handy for, you know, helping.

PSH. Holding retractors

PEP. Yes, all that sort of stuff but we had of course wonderful sisters, staffs [?].

PSH. I get the feeling from both what you have said and what you have written that you have always loved clinical medicine and I am trying to see, now how was it that, when you were really very much fulfilled in some ways by this, that you came gradually back into research?

PEP. Well I think that is perhaps part of what I had, shall we say, in my imagination, planned for myself. I wanted to do research. Although I was interested in medicine I was interested in medicine also as a biologist, and hence also if you like, my interest in genetics, or through my interest in genetics. So it seemed to me that medicine needed a biological scientific input in order to get on, in order to move forward, to begin thinking about the next century if you like, you know very remotely of course. And consequently that was part of my aspiration. In addition, I was extremely lucky because my first boss, that is to say as soon as the war was drawing to an end and consultants started coming back from the front and so on. My first boss was

Richard Ellis, who eventually went to Edinburgh as Professor there of Child Life and Health, and he took a liking to me and he thought I ought to do research. When he was about to leave and go to Edinburgh, he handed over to Philip Evans with comments to the effect 'look after this man. He ought to be doing research'. Undoubtedly I was clinically OK, because the Evelina had really given me a bit of a spine for what practical medicine meant. So much so that when I did my ..... first of all my DCH, above all when I did my membership, with Philip Evans pushing me to do it, he said "but you are ready" and I said "no I'm not" and he said "yes you are. Go on". So I went and I passed and that was, you know, the beginning. So I had really finished by then the main background shall we say for entering medicine, but from then it went into research mainly, because first of all I had a fellowship for 2 years.

PSH. That was now at Guy's?

PEP. That was at Guys now, yes that's right. I finished in the Evelina in '48. At the Evelina I finished in '48, then I had 2 years 'till 1950 as a Research Fellow for the National Birthday Trust, during which time I did work on kernicterus, clinical work and then some experimental work on rats and so on.

PSH. And then am I right that it was at that point you managed to link with Maurice Campbell and the congenital heart work?

PEP. Yes, it was in fact Maurice Campbell who talking over lunch as they always do, with Phillip Evans, said I need somebody to give me a hand with the material which I have. Because at that time, Guy's and Hopkins were linked together and congenital heart disease in both places was beginning to be very important, and the treatment of it etc and so on. So Campbell wanted somebody to give him a hand with sorting out the material. And Phillip Evans said "well why don't you try Polani. He is doing this experimental kernicterus, but he has got spare time". So I got involved in congenital hearts. And that was really a great blessing; at that moment too I realised that I needed an input into genetics, into modern genetics and so I tried to arrange, and I managed to arrange to have a moonlighting kind of arrangement with Penrose, at the Galton.

PSH. That was something that interested me a lot and I didn't quite appreciate that and I mean, that must have been hugely important because . . .

PEP. Terribly important.

PSH. I suppose outside the Galton, and certainly in Guys at that point, there was nobody else really who was interested in genetics.

PEP. No. There were of course people who were with Payling Wright [e.g. Peter Gorer] in pathology and very interested in immunological systems particularly, and therefore in, a sense, genetics. And we had quite a lot of talks on genetics at Guys by people who were working in the area, but as you say, there wasn't anybody systematically doing any work there. Whereas Penrose of course was perfect.

PSH. I never knew Penrose well, indeed at the time I came back from America he had already retired, and some people seem to have found him quite easy to approach and others less easy. How, did you find that he was somebody that you could link with easily at a distance, like you were? How did it work out? I'm intrigued.

PEP. Well in practice I spent all my spare time at the Galton, shall we say 'sitting at his feet' if you like, but I mean you had to do that, because Penrose was not a man that was given to a great deal of effusion, so you had to pick pearls as they happened to drop out of his mouth and you had to, yes, but once he saw what I was doing with congenital hearts he then got interested himself, involved in that, and he said why don't you unravel things like maternal age, paternal age, of course all this sort of stuff, parity or something. Then he volunteered quite a lot of information on the statistics, which was his forté so to speak. He was a statistician with an eye to simplify matters. He wasn't a great friend of course of Ronald Fisher, but he was a very, more handy statistician. One that could handle simple statistics. And so anyway he got very interested in that, and in a sense it was an encouragement; but as far as I was concerned I mean, congenital hearts proved to be very important because of the coarctation of the aorta study.

PSH. So did you start, I am thinking now in terms of the link through coarctation with Turners. Was coarctation one of the congenital heart defects which you were looking at in terms of surgery or how did it happen?

PEP. No, exactly for the reason it wasn't, if you like, in the sense that everybody was then thinking of Fallot's of course, and then thinking about holes in the heart of various types. But coarctation wasn't yet on the surgical books in the early days.

PSH. That's interesting.

PEP. You know

PSH. I didn't realise that. I imagined you could repair a coarctation before you could repair a hole in the heart.

PEP. Oh probably yes, but somehow or other coarctation wasn't one of the things that people were thinking very much about, also because in a sense it was less life-threatening probably. So in dealing with the material which Maurice Campbell had accumulated, I was left with a bunch of about, I forget exactly, let's say 15 coarctations, which I didn't know what to do with because there were too few; but we had an idea then already that it was a male malformation, because out of those 15 I would say, I can't remember the figures, I think you will find the figures there you know, what I have written. I think probably, say 10 were males and 5, I doubt if there were 5, fewer than 5 were females. But four females I think and of the four females, two or three had ovarian agenesis and they were thought to be Turner's syndrome, webbing of the neck and all the rest of it, small and so on, and they weren't children of course, they were already young adults. So the question that came to mind first was whether this was a mimic by nature or the other way

round.....let's say a mimic by nature of the Jost experiments of the castration of rabbits, where if you castrate a rabbit it turns out a female phenotype.

PSH. Yes.

PEP. And I wondered whether these were in fact originally males who had lost their ovaries, because in those days we thought they didn't have any ovaries: in fact, ovarian agenesis was their classification. And so how to test for it was a bit of a problem, but we decided just to use Barr's body, which had just come off the production line as it were, and I did that work with Hunter and Lennox to whom I sent specimens, which I had already examined myself but didn't trust my judgement.

PSH. Did you have a lab at Guy's then or?

PEP. Yes I had, there was an inter-departmental laboratory which was a new idea for Guys', which was extremely handy. So I collected, I think 3 or 4 bits of skin, sent them to Lennox and said, would you please tell me what you think about nuclear sexing of these bits of skin; and time went by and nothing happened. And so one day I rang him up and said "what have you done. What have you made out of those specimens?" He said "they are not very interesting, just ordinary males". Exactly what I wanted! But the second thought, as soon as he said that, I started thinking really more seriously and I said "right: well what is the evidence that they are males?" Because we knew that males could carry a Y chromosome and we knew that we were testing only for the X through Barr body testing. And I just wondered whether there might be XO, and in order to confirm that they had only one X chromosome at any rate, irrespective of whether the other one was missing or was a Y. I thought about using some sort of genetic marker on the X and haemophilia was one which would be too rare to use, but colour blindness seemed to be OK; and when I discussed it with Penrose he said "Oh yes colour blindness would be fine, because about 7% for males and so on and 0.5% for females, so you would be alright if you have enough patients". So I got enough patients; I had been helped by Sir Robert Platt, who then was Dr Platt.

PSH. Right.

PEP. and other people who gave me, and Peter Bishop particularly, at Guy's. So I got my 25 patients and out of those 25, 3 were colour blind. And there was a nice story there. A personal story attached to it, because I turned out to be colour blind myself, which I didn't know.

PSH. Yes. Because colour blindness had been used quite a bit. I was thinking of Julia Bell's study with Haldane. Was Julia Bell still at the Galton?

PEP. Oh yes. And Haldane was there.

PSH. And Haldane?

PEP. Not at the Galton.

PSH. No but in London. At University College.

PEP. University College yes.

PSH. And Ursula Mittwoch.

PEP. Oh yes. Indeed

PSH. And who presumably already at that point was doing chromosome studies of some kind was she? Or maybe not.

PEP. Not really I think. You know the story of the Mongols.

PSH. I do. Yes

PEP. But they were meiotic studies which was in fact, shall we say, the bread and butter of cytogeneticists, of human cytogeneticists: it was to do meiotic studies because they thought they would easily see in spermatogonia, the cell divisions and therefore count chromosomes. Which was a lost cause of course, because the real advance came when they started culturing cells from somatic tissue and then blocking mitosis.

PSH. So I am trying to think then, which year have we got to in terms of - you have identified that. . .

PEP. My first thing was '54.

PSH. Right. That was with the Barr bodies

PEP. That was with the Barr bodies.

PSH. And then the male pattern of colour blindness?

PEP. Oh that came in the year, 2 years later, '56.

PSH. '56, and then of course the normal chromosome number also in '56

PEP. also '56

PSH. And I suppose the thing that is in my mind is that there was this interval of nearly 3 years between establishing the normal human chromosome number and the first reports in abnormalities, which all seemed to come out in that very special year in 1959.

PEP. That's right.

PSH. And what I am just wondering is, in between those two points,

PEP. What happened? Yes. Well various things happened. As far as I am concerned, '54 I got this thing, then I said immediately, well while we are getting enough material to do the colour blindness testing, which meant

getting 20 or 30 patients lined up, which didn't come easy because Turner's syndrome is not very common.

PSH. No. Indeed. I am amazed you were able to get

PEP. Well eventually because of Robert Platt, because of Peter Bishop and so on, we got the cases. But in the meantime however, I thought that I would try my luck at chromosomes. So I went and saw Payling Wright, it was 1954 already. I went and saw Payling Wright and I said "Look Professor Wright, how do I set about it?" And he said I can't tell you but I tell you what we can do. I suggest you contact the chap, I forget his name now, oh dear. Oh anyway, who was doing tissue culture in Guy's. So I contacted him and he decided yes, I will give it a try. He had all the material for culturing skin and so on and so forth. And so we got together and some patients, 2 or 3, not many, 3 or 4 patients with Turner's syndrome. And then we did a few controls. I must say that our success with tissue culture was miserable as far as chromosomes were concerned.

PSH. Gordon Thomas. Is that it?

PEP. Gordon. That's correct – sorry – thank you. Yes Gordon Thomas, who actually was a very nice chap and very good but dealing with chromosomes was not his cup of tea. However, we did manage to see chromosomes. We did manage to count even one or two cells but we never got to very high numbers. Anyway, and if we got, I think we got a few 45s

PSH. Yes

PEP. Many 44s or so on but we were still up against the dogma of 48.

PSH. 48. Yes so you, you never – you still feel . . .

PEP. We said broken cells, we really could not sort out the overlaps, and so and so forth, you know there was all sorts of problems.

PSH . It amazes me again and again how this comes up, with people either finding too many or too few, and again this entrenched thought that you felt that you should be getting up to 48 or something like that and you weren't.

PEP. We were thinking about 47 for Turner's say, you see, and 45 and I think if I'm right when we got these numbers around 45, it might have been easily control as well as Turner whatever, so really our uncertainty about the quality was the problem. We didn't get enough spreading, it was always difficult to deal with it: bi-armed and acrocentric chromosomes which we then didn't know about.

PSH. Were you trying to do quite a lot of this yourself.

PEP. Oh yes, with him. He was really pretty good at the culture side.

PSH. And then, you did the actual . . .

PEP. I did the looking at the microscope, yes. Also, because don't forget I had finished my work with kernicterus in rats, so I was quite good with the microscope. Well I mean I was quite good because I had learned how to handle a microscope. We had good microscopes. [Cooke, Troughton & Sims]

PSH. And then when was it you made the link with Charles Ford?

PEP. Oh Charles Ford I had met before, quite soon after my first paper in '54 with Turner's syndrome on the sex chromatin. And then we arranged a meeting, a symposium on nuclear sexing, to which he was particularly invited because we knew that he was good with chromosomes of mice and we wanted him to spread his hand, his technique shall we say rather, his spreading technique to humans. So we thought if we invite him we might persuade him that there is something to be got out of these humans. Also because incidentally, before I contacted Ford, I contacted, well for a long time I didn't use his name, but I think I can use his name, P C Koller, who then was working at the Royal Marsden opposite the Brompton and ..... I had never met him before, but I went and saw him and I said look, I have this evidence of colour blindness which is now coming out. There is a story of sex chromatin and so on. I think we ought to look at the chromosomes and you are an expert on chromosomes. Why don't you do some of it yourself or perhaps have one of your PhD students look at it, and he said "No. No. No. I mean, we all know that sex in humans is like Drosophila.....

PSH. Yes

PEP. "looking about something you know" he said. And then I went as far as I could for Ford. And then Ford published with Laijtha the first chromosome results on human bone marrow on Klinefelter, they thought was an XX. By then we had done also colour vision studies on Klinefelter, so we knew that they had two X chromosomes at least. We didn't know they had as well Y. So as soon as he published that, because we were in contact, I sent him material from Klinefelters and Turners, but that was already '58 because that paper was published in 1958 and I had seen a preview they had sent me: both Laijtha and he himself had sent me previews of the paper. By then of course Ford was already convinced that there was something to be got out of human chromosomes. And anyway, while he was working on this material which I had sent him, Pat Jacobs was working on a Klinefelter in Edinburgh and I went to Copenhagen, because I was attached to the World Health Organisation then to work in the States, and they were sort of indoctrinating me in to what I should do in the States and so on. And while I was there I was in touch with Westergard, the geneticist in Copenhagen and we discussed of course sex determination and all that sort of matter and then I re-read the paper of Ursula Mittwoch So here was the idea that even mongols might have something funny. So post haste I telephoned Charles Ford. We met at London airport, we had a quick discussion, planned what to do. By then we knew that the Turners were XO and we knew that the Klinefelters were XXY, or at least they were mosaics in our case: and non mosaics in the case of Pat Jacobs. So we thought of mongolism and at the same time we said well, let's sort out mongolism like this, straightforward, and then let's look at mongols born from young mothers, where there is familial tendency. That was all planned in January of 1959. And then we published these results.

And in '59 we published, also, or at least we got hold of the mongol. By then of course Lejeune had published his story of mongolism.

PSH. Yes

PEP. and so we were left with the mongols born from young mothers. We found a girl with 46 chromosomes but with a translocation.

PSH. It is amazing to me then, how rapidly all these things seemed to sort of happen almost at once, with maybe 3 or 4, even maybe 5 groups all reaching the same point. Perhaps that was just because the technology allowed one to get . . .

PEP. Absolutely. Absolutely, it was entirely a matter of technique. When Tjio and Levan published, already by then of course - was it Kemp in Denmark who started the tissue culture business to do with the tissue culture?

PSH. I think so.

PEP. Anyway it was from Denmark and he had the idea, the correct idea, that the best way of getting the chromosomes was to do them in dividing cells in culture. And then of course colchicine, colcemid, hypotonic, squashing, all that came in and all that was the thing that gave the chromosome number, the exact chromosome number and the details.

PSH. At what point did you manage to convince Penrose that human sex determination was different from Drosophila.

PEP. Penrose would not have it. Penrose would not have it, I have to say. He was annoyed with me. He said 'where do you get this stupid idea?' And I said 'well yes Professor Penrose, but see the figures would suggest that there is something'. 'Yes but you know, I mean all sorts of ' . . . Well anyway, when I sent my paper into the Lancet in '56 I had the audacity not only of suggesting that they might be XO sex but also writing that, if they were XO sex, if indeed they were XO sex they would be unlike what happens in Drosophila. Here were female XO sex where it was officially male. So perhaps sex determination in man was not correctly interpreted in those days. And the Lancet wouldn't have this bit. I think I draw the parallel, or the anti-parallel, with what happened when I originally sent the 1954 paper to Nature.

PSH. It's too clinical.

PEP. Too clinical.

PSH. You can't win.

PEP. 'What's this story about', you know. 'These Turner females. What have they got to do with . . .'

PSH. Do you think the Lancet might have got Penrose's views on . . .

PEP. I don't know. They certainly got some views and I know that they were quite determined for me to alter this bit, because the editor then, rang up Philip Evans, whose friend he was, and he knew that I was working for Philip Evans, and said " No we can't have that sort of thing. Get him to modify it. Take it all out". And I said "No. I'm not going take out the XO sex story". Anyway that's another thing.

PSH. I mean, it is a wonderful sort of chapter, the whole area of these sex chromosome abnormalities and, when you had got on top of that, were you already starting to think in terms of - I am trying to think the year when you actually were given the research chair at Guy's. Which year was that?

PEP. 1960.

PSH. So that came really quite shortly after all this series of studies.

PEP. Ah yes. Yes I see

PSH. But I suppose what I'm thinking is that, were you exclusively working on those or perhaps I suppose your kernicterus work had already given a basis for the cerebral palsy foundation of the Guy's unit. I don't think they gave you the unit just because of the sex chromosome abnormalities did they?

PEP. Well now, the story is – it's one of those stories. Let me start really perhaps . . . Let me go back a moment.

PSH. I hope I'm not tiring you Paul. Say when you are exhausted.

PEP. Oh no no no no no no. Stop me if I ramble.

PSH. Not at all

PEP. Please because.....

PSH. as long as I'm not wearing you out

PEP. No no no no no no, not a bit. Now what happened, I was assistant to the Director of Paediatrics at Guy's, Philip Evans, from 1950 to 1955. And in 1955 I was looking for a job here and there and I didn't get this and I didn't get that. Let's forget about that. It's not important.

PSH. It's interesting though how not getting a job sometimes is a tremendous benefit with hindsight.

PEP. With hindsight I find it absolutely incredible of the good luck . . .

PSH. You would never have developed things as you did if you had been part of the Great Ormond Street set-up rather than able to do it at Guy's perhaps?

PEP. That's right, except that I will say this, that I very narrowly missed getting the Readership at the Institute of Child Health, at the Institute, because by then the story of the XO sex had come out, only just, but a number of

people on the committee wanted me to..... would have liked me to get the job. But I think really, yes in conclusion I was very lucky I didn't get it. Now, what happened was in '55, while I was looking for a job the Spastics Society, who were then beginning to accumulate money for research, well money for treatment really, money for handling of spastics and wanted to establish themselves in the role of people who looked after spastics and after the interests of spastics. They wanted to put spastics on the map. When that happened they were looking for somebody who would do a little bit of fact-finding research on spastics. How many there were, how were they handled by the medical officers of health of this and that districts, as opposed to the other district and so on. I thought I would apply for that and Ronnie McKeith, who was in the inner circle of the Spastics Society supported me very strongly. So I got the job, as I said, Research Physician for the Spastics Society. And then my job consisted of going around England, Scotland and Wales and so on, and Ireland, to look at spastics and to get a feel of how they were being handled and what was missing in terms of education facilities, treatment facilities, whatever. And all that was fed back to the advisory committee, the medical advisory committee of the Spastics Society.

In the meantime the World Health Organisation had contacted the Spastics Society because they wanted, because the Americans had started a pregnancy wastage programme with 40,000 mothers enrolled right through pregnancy and so on and so forth. And they wanted, the W.H.O. wanted to have an observer there, somebody who was in the cerebral palsy field, because the original idea of 40,000 pregnancies started from cerebral palsy, at Hopkins. So they said, and this was the Spastics Society said they would second me to go to W.H.O. and then W.H.O. sent me to the States. I went in '59. I have lost track..... But what you really wanted to know was how the spastics got into that. In the meantime, while I was in the States, the Spastics had accumulated quite a bit of money and they wanted to invest that money partly in research, and the Chairman of the Spastics Society, the Director, C P Stephens, Dawson Shepherd was the Chairman, wanted to..... they had the idea that they wanted to tackle the problem of prevention and therefore look at the basics of the origin of cerebral palsy. And when I got back from the States, having finished the job for the W.H.O., the Chairman of the Spastics Society asked me to prepare a blueprint for something that would be a programme of research. By then they had established a very good committee, Research Advisory Committee at the Spastics Society. They looked at my plan. There were two ways of dealing with the problem, either giving money to established units or to establish a unit per se. And I think it was Penrose who then said, "well we had better establish a unit because it would have several advantages at some point", not important really at this moment. And eventually the unit was thought of and established along the lines which I had put forward. It was to be a multi-disciplinary unit. It was to have a genetic philosophy because genetics was on the move. I was certainly in favour of that and I thought we would have a multi-disciplinary unit which would look not only at cerebral palsy but across the border into developmental disorder generally.

PSH. I am amazed that then charities and other bodies seemed to have the flexibility to really get something big like that off the ground without all the sort

of delay of committees. Now it seems that anything like that would have to take years and years for it to actually ever happen . .

PEP. Yes

PSH. If it ever did. Must have been some people of great vision

PEP. Well I think Dawson Shepherd was that kind of a man. Of course the director of the Spastics Society, C P Stephens, who was a medical man, was also quite easily convinced and later on of course Tim Yeo was head of the Spastics Society. He was at the helm, at least as a director I think. So yes, people had then this vision. It wasn't everybody in the rank and file who were enthusiastic about it. I think, however, the directorate, so to speak, were really quite unanimous over that.

PSH. So which year was it that the new unit opened

PEP. At Guy's?

PSH. AT Guy's yes.

PEP. 1960. October 1960. It was established in October 1960. So yes it was very quick. You are quite right. It was extremely quick.

PSH. Yes. I don't think this is the time to go into how the unit grew and developed, but it is amazing how it has and I guess that is must be something of which you are hugely proud, that it grew from yourself and then into something that was very substantial and standing on its own feet.

PEP. I think we were lucky. We were in the, I think essentially because were in the right business. And the second thing which was very important I'm sure was that we should have right away, as soon as possible, an input into practical matters, so that we would link, so that the unit would have to have two arms. One was a research arm and the other was an applied arm through genetic counselling and so on. Because by then you see, chromosomes were beginning to be used for diagnosis. And consequently later on for pre-natal diagnosis, particularly with the translocation mongolism story, which implied the possibility that genetics might be involved at chromosomal level in the origin of some developmental defects.

PSH. Yes

PEP. If so, then perhaps there was a chance of doing something about it even prenatally so that counselling would cease to be entirely crystal gazing.

PSH. absolutely

PEP. Crystal ball gazing if you like or abstract in any case and certainly based on statistical facts and so on. It could be something actual in relation to that particular individual, in that particular plane.

PSH. Can I ask, in terms of getting the NHS involved, because I mean that was a real achievement, quite unlike any of the other London centres especially, that you seem to have got this very early involvement of the NHS and not just in London but the whole of the south east region. Was this something that happened easily or did you have really to put a lot of effort into getting that to happen?

PEP. I think the secret was the proof of the cake. In this sense, that I argued, with my colleagues too, that to do the clinical side, the application side, genetic counselling and any prenatal diagnostic things which were in the offing, because I mean it was something that was only just being considered, we had to demonstrate its usefulness, or at least its feasibility first of all and then its usefulness. And I argued therefore that given that we had enough money from the Spastics Society, that we should invest a proportion of that money into the practical uses, and so we did and for two or three years, I forget now exactly how many, we ran a service, a genetic service with research money, which was essentially research money. So that was a pump-priming operation, in a sense, which then when it turned out to be useful, we convinced the Department of Health that here they could have something going and should contribute. So that was the first step. The second step immediately after that was the fact that we were able to secure the supra-regional laboratory for inborn errors of metabolism, which was also then associated to the unit through the biochemistry group of the unit, Philip Benson, Tony Fensom and so on.

PSH. Yes

PEP. and the cytogenetic side was then split off, the research side from the applied side. But that all happened gradually. Then of course a very important moment was when Fraser Roberts retired from the Hospital for Sick Children, from the Institute of Child Health and the MRC unit. When he joined us and he did the genetic counselling; and that was in fact, shall we say, the nub of this wheel of genetic counselling.

PSH. Do you know I had completely forgotten that Fraser Roberts had joined you from Great Ormond Street. That must have been I suppose the

PEP. '64 I think

PSH. '64

PEP. About'64

PSH. I suppose then he must have carried on until Caroline Berry started?

PEP. Oh yes, Caroline Berry was appointed fairly soon after that. Caroline Berry was appointed fairly soon. That was one of those things, I was talking to Sam Berry at a meeting and he said "My wife is looking for a job" I said "oh wonderful."

PSH. One of the things, quite different Paul, I wonder whether I might just ask you is, you have kept very strong links with Italy and you have had very

talented colleagues who have come over from Italy and made their careers here. And you still visit Italy quite a lot don't you?

PEP. Yes I do.

PSH. Do you have a home there or . . .?

PEP. I have a flat in a small town called Udine, which is very near Trieste where I was born. Yes I can tell you the secret about that. It's not a major secret. Well let's tackle one thing at a time. Let's tackle first of all the colleagues, what you might call the Italian Mafia. Forgive me. But my colleagues at Guy's often pulled my leg over that.

PSH. Yes, but always very kindly!

PEP. Oh yes of course, and well, Giannelli who then became Professor of Molecular Genetics of London University, joined me right from the beginning in 1960 because I gave a seminar on chromosomes in Rome to Montalenti's group, when Professor Montalenti was geneticist at Naples first and then Rome – and he ran a very successful unit too in Rome. And I gave a seminar on chromosomes, which had only just been 'discovered', it must have been about 1959 or 1960 perhaps. No sorry, 1960. And Giannelli, who had done a thesis on congenital heart disease in pathology, was in the audience; and when the lecture finished he came to me and said "Professor, could I come and learn a little bit about the techniques?" I said "well if you can find the money you are welcome to come". He found himself a bursary from the Italian Government and came to the unit and stayed. It's as simple as that. He would turn out to be a very good worker, very reliable and did a lot of imaginative work and so on. He had three different skills in his lifetime; three different scientific skills.

PSH. It's amazing how many people come to a place to learn something for a few months and then stay for the rest of their careers.

PEP. That's right. That's what it is and you see he retired two years ago.

PSH. Yes.

PEP. Adinolfi was another person. Adinolfi was also one of Montalenti's boys, and he went to Leiden with Siniscalco, Professor Siniscalco in genetics; and then from there he came to London at Mary's to work on blood groups in the MRC unit there. And from there, when I was looking to expand the immunology group, which had only started at Guy's within the unit, he applied for the job and he was very qualified, obviously very qualified: and he got the job and he turned out to be a very good, very successful, very good. So you see the unit was essentially - we had cytology, biochemistry, immunology - they were the basics, basic groups. Originally we had also quite a sprinkling of epidemiology and so on. Sorry. You were going to ask me something?

PSH. Paul, I was just thinking, in all this series of work, is there anything that sort of stands out in terms of the one thing which gives you the greatest

pleasure to look back on in terms of your research and career? Is there anything . . .?

PEP. Oh, undoubtedly the sex chromosomes. That is another, the thing which was, shall we say which I consider more important, because we revised the idea of sex determination in man. The Y chromosome became suddenly very important and so on and so forth. So that was undoubtedly the key. The other thing that was interesting too was when we started doing work with Mary Seller, on using the observations that mosaicism leads to a dilution of the non-mosaic effect, because if you have two populations of cells, normal and abnormal, the individual who carries these two populations is intermediate quite often, one way or another. Looks a bit like a mongol, a mixture of mongol and normal and so on and so forth. So with that idea in mind we thought perhaps we could think of using cells in order to remedy certain defects, genetic defects, at cell level. And we did some experimental work there. That was quite interesting, very interesting in fact. And then we had the work on spontaneous abortion and all that stuff you know.

PSH. Yes but the sex chromosomes . . .

PEP. As far as I am concerned for me . . . Yes for me that was the main thing. That and the second one was probably, still in chromosomes, was the mongol with 46 .....

PSH. The translocation

PEP. The translocation mongolism

PSH. Because that really was, well that was again was a particular contribution of yours.

PEP. Oh yes

PSH. Paul, I think I have probably worn you out.

PEP. No you haven't. Not at all. No no.

PSH. I have covered all the things which are down on my piece of paper I think except, just to say, I can't finish without just mentioning your hobbies and the riding. Have you always been a keen horse rider, or did you take it up when you came to this country.

PEP. No no no. It takes me back to when I was a relatively young boy probably, 10 or thereabouts. You may not know, but very near Trieste there is a small village called Lipice.

PSH. Yes I do

PEP. You do. Wonderful.

PSH . I was in Trieste actually in September.

PEP. Did you go to Lipice?

PSH. No sadly I didn't but I

PEP. Well Lipice now is in Slovenia.

PSH. Yes

PEP. Well Lipice was the stables of his Imperial Majesty the Emperor of Austria and that's where the white horses, the Lipizzaner horses are bred, in fact the name Lipizzaner comes from Lipice.

PSH. Which I suppose now are mostly in Vienna.

PEP. Now in Vienna, in Piber near Gratz and so on. That's where they have the pastures and so on. When I was a young boy, some of us had the idea that we would like to see these horses a little bit close by. We saw them in carriages. We saw them in things of that sort and so we used to go to Lipice on Saturday or Sunday, at weekends, when we could, when we were free from school, and offer our services to muck out.

PSH. Right.

PEP. And in return for that they would let us ride the mares, not the stallions, the mares back from the paddocks. And you know that's how it started. I mean, I must have done it a few times, it wasn't anything very consistent, but it was enough to get my appetite going for riding, yes

PSH. And then did you take it up again when you made a home out here in Guildford?

PEP. Yes. Even before. We, well that's another story. My wife worked during the war at the BBC in the European services of the BBC, in the Italian section. And at a certain moment in time, because of her interest in riding, she thought that she ought to start a riding club at the BBC. She found out that the Civil Service had already established a riding club. So they associated the BBC to the Civil Service riding club and then we found out that the Civil Service riding club had horses of their own in stables near Hyde Park and you could ride in Hyde Park. And then we joined, through the BBC club, we joined the Civil Service riding club and then we rode the horses and then eventually we bought one of the horses. Some club members used to buy a horse, and the society, the club, would keep the horse and you would have the right to ride a couple of hours a week or something. Anyway

PSH. So already in central London you could ride

PEP. Oh yes, we used to ride.

PSH. And I guess that must have been one of the reasons when you were settling that you came out here, that you would have space for horses?

PEP. Yes, in fact originally we had horses at a farm very near the Royal Horticultural Gardens at Wisley. Very near there. We had horses.....we had a horse. Yes we played around with horses.

PSH. finally Paul, you look very active. On the table before we started there were lots of books and journals, you are obviously keeping very very much in the swim of things.

PEP. Well I try.

PSH. Yes, all of us try. It is not quite possible, but do you find that is important and enjoyable to see how things are developing now?

PEP. Yes. I am very lucky too, that I have an honorary attachment to the unit which I used to run and consequently I have facilities; I can get access to the library and so on.

PSH. That's nice.

PEP. I write a little bit and I lecture so to speak.

PSH. Did you say write or ride?

PEP. write

PSH. You don't ride now?

PEP. No. I don't ride now. The horse that we had, the last horse that we had, was a horse that we bred ourselves and he was really my wife's horse and when my wife was very ill, at the end of her illness, the last few months, she was actually afraid of the horse. Had become suddenly afraid of him and wouldn't go and see him any more. And the horse took that to heart, I think, and within a month of my wife dying he was dead also. He stopped eating: and, you know, there was nothing wrong with him physically in a sense that the vets could see. Anyway so yes, no I don't ride. That is of course, we used to ride. We liked to ski. We had a reasonably active life.

PSH. But you write and read.

PEP. Yes I do. I write a little bit. I read. I have an idea, I had an idea of writing a little booklet, on very simple, not genetics per se but more really DNA. Something that anybody could pick up and get a general understanding of it without having to know necessarily all the details, just have a smattering of what it does.

PSH. Have you thought of writing a biography, an autobiography of yourself?

PEP. No. No I haven't. As far as I have got is here. That's as far as I've got, those pages which I have written. I don't think you know, yes I mean, it makes a story

PSH. If you have time to do it ever, if you ever have time to do it, people would find it very interesting.

PEP. Well thank you. Thank you for saying so but I think, you know, too many things that happened in life are really so much – chance. I don't know how to, ...

PSH. Yes that's true.

PEP. how to describe it better than that. I mean the chance that I came to England. The chance that I came at that time. The chance that I would find a job as a ship's surgeon. The chance that I would not be on the Arandora Star. The chance that I didn't get the first job. The chance that I didn't get the second job. The chance that I got the Spastics Society to accept me and the chance that I had a very good time in the States while I was there, which undoubtedly was a contributing factor to my development and also to, and also in a sense to favouring then, my entering the academic circles here. So many elements of chance. And then the greatest chance, that I found my wife, probably and so on you know.

PSH. Paul, thank you, it is a privilege. Thank you and I hope I haven't tired you too much.