

# Josué Feingold



## Personal Details

Name	Josué Feingold
Dates	1933(?)-2016
Place of Birth	
Main work place	Paris
Principal field of work	Mathematical and Human Population Genetics

## Interview

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### **Interview with Professor Josué Feingold in Paris, Monday 18<sup>th</sup> April, 2005**

PSH. It's Monday 18 April 2005 and I am talking with Professor Josué Feingold at Hôpital Necker in Paris.

Josué, I am very grateful for your spending time and might I ask what was it brought you into medical genetics at the beginning? What factors . . .

JF. It was in the 1960 – 1975 years; I was studying to be a paediatrician in

Paris hospitals and then I saw that genetics must be something important so for two years I learned genetics, not at the school of medicine but in the faculty of science in Paris.

PSH. At Sorbonne?

JF. It was not Sorbonne. It was near Sorbonne in a small laboratory where I had excellent teachers in genetics, Boris Ephrussi. M.Gans and M Rizet and this was for the first year and I was a student with Roland Berger. I met him because he was working at this time with Lejeune. This was the first year. The second course was two or three years later. It was a course on what we call quantitative genetics and the book of Falconer in this field and I had many lectures by Malécot on information genetics. So I learned much quantitative and population genetics and we had one course on medical genetics was made by J. Sutter. Sutter was the chief of department of genetics at Institute National des Études Démographiques and Sutter made many studies on human genetics, in particular the effects of consanguinity. He made monographs on eugenics and consanguinity. When he retired Albert Jacquard was chief of this department. And this department did a very good epidemiological study, one by Goux on the dislocation of the hip.

PSH. Jean Sutter.

JF. He died about 35 years ago.

PSH. Can I ask you Josué, was there some particular reason why you became interested in quantitative genetics. Had you previous mathematical experience?

JF. Yes, when I was in Lycée I was in the branch of mathematics and I learned some statistics and epidemiology with Daniel Schwartz who introduced epidemiology into France, before studying genetics.

PSH. Did you encounter at that early stage the work of Fisher and people like that?

JF. Yes. Fisher, Haldane, Sewall Wright.

PSH. OK. So you were familiar with those aspects of genetics before entering medicine.

JF. No, not exactly. Because in France the medical studies are very long, I became what you call a Resident in paediatrics and during this period I learn genetics, some statistics and epidemiology,

PSH. But your mathematical interest goes back to your time at the lycée?

JF. Yes

PSH. Because not many medical doctors have good knowledge of mathematics and I think you are one of the exceptions.

JF. The reason why I met my wife is because she was a student in mathematics, but she became a geneticist and worked about 7 to 8 years with Jean Dausset. Catherine Bonaiti is like me, she is a physician but she learned statistics and population genetics. Francoise Clarget is a mathematician and turned to quantitative genetics and epidemiology.

PSH. Can I ask you a little about Malécot because he has had a big influence on statisticians generally but I don't think had the same influence on people perhaps in genetics.

JF. No he was more known in the United States and Great Britain than in France. When he died, in the newspaper there were two lines. He never became a member of the Academy of Science and Malécot is known by very few people in France.

PSH. That's interesting. And am I right that Malécot himself did not apply his work directly to genetics so much, but was he much more in terms of general statistics or . . . ?

JF. No. I tried to find for you, his first book was in 1950, it is called the *Mathématique de l'Hérédité*. His thesis was on inbreeding, so he put mathematics and genetics together. But he was only known by some population geneticists in France. Newton Morton made him known in the English speaking populations.

PSH. That's very interesting. So after you had done these courses in basic genetics and mathematical genetics when did you start to actually work in human genetics?

JF. I came and discussed with Jean Frézal here, and told him my interest in applied genetics. After some discussion I came to work in his laboratory in 1967.

PSH. Was that '67?

JF. '67. In '77 I had my own laboratory near Boué on genetic epidemiology.

PSH. So '67, yes, which was a time when things were starting to develop rapidly.

JF. It began here. During this period in the Children's Hospital I studied many malformations and we worked with Cedric Carter and we made what he made

in Britain, the familial study of some malformations. But if you take the past, genetics was introduced in Hôpital Enfants Malades by Maurice Lamy and Robert Debré. Maurice Lamy had three geneticists Maroteaux, de Grouchy and Frézal, and Frézal was one year in London at the Galton laboratory. At first they made a study on pyloric stenosis. This was a very old study, and the first I think was not published in a great paper, Jean Frézal can tell you more about it. Jean Frézal had written an interesting paper on the genetics of diabetes. And the term was not a polygenic inheritance but he said many genes can be at the origin of diabetes and this in the 1960s. So when I came to his laboratory we studied many malformations and diabetes also. I worked with Marie Louise Briard and Catherine Bonaiti. Catherine Bonaiti who spent one year in Edinburgh, near Falconer's laboratory where she learned many statistical genetics methods and applied them here when she came back.

PSH. Can I ask Josué, when you formed this laboratory was it a purely mathematical laboratory or did you have genetic marker typing?

JF. We made many population studies. The markers were studied in other laboratories.

PSH. So it was not just a theoretical group.

JF. Not a theoretical group. We made these studies in the French West Indies.

PSH. Including the ones on . . . ? No I'm thinking now of Réunion, I'm thinking of your muscular dystrophy studies, that was later.

JF. In the French West Indies, there was a problem on the small island called St Barthelémy a problem of deafness, so we made a very big study on deafness and this was analysed by Catherine Bonaiti. We thought that perhaps this disease was recessive and then we made a study on the frequency of congenital malformation in Guadeloupe and we made new studies on another island which was La Desirade. We studied hypertension and leprosy. It was Laurent Abel, it was his first study on leprosy on La Desirade but unfortunately we had no possibility to have some lymphocytes.

PSH. So you couldn't do HLA?

JF. No. So after that he continued and made a study in Vietnam with a group from McGill on leprosy.

PSH. Can I ask, at what time did you start your study on haemochromatosis. How did that come about? Was Saggi a gastroenterologist or hepatologist or physician?

JF. No, Saggi was a biochemist but he was also a physician so he was seeing

the patients and curing them. So he was doing biochemistry and some clinical medical genetics. This came about with the research that was in George Shapira's laboratory called the Ramon study. Ramon Saddi called me and told me there is something wrong. There was a great paper with Shapira, Jean Frézal, Robert Debré that was published in the Annals of Human Genetics, and they said that the disease was dominant and Ramon Saddi told me that it was not possible. It must be a recessive disease, so we made this study and it was easy to show that this was a recessive disease.

PSH. And was this in Paris or was it in the West of France?

JF. Here, in Paris.

PSH. Here OK. Here at Necker, because I had it in my memory that there was some connection with Brittany.

Now you bring up Lalouel, can I ask you the connection between Lalouel and there are some other statistical geneticists. Did they have their beginnings in your unit or was this separate?

JF. Lalouel was in Lejeune's lab and he made a very interesting monograph on small populations and then he went to the United States for about 10 years in Hawaii in Newton Morton's laboratory.

PSH. Right.

JF. And then he came back to France and was Professor, not in the school of medicine but in the faculty of science at Paris University VII but it was difficult. He was working with Marc Lathrop, he wasn't happy in France and returned to the United States at Salt Lake City. Marc Lathrop went to the laboratory of Dausset.

PSH. That's where he had his training originally, Marc Lathrop?

JF. No, Marc Lathrop came from Canada. He was a very good geneticist. He liked to live in France, so he was with Lalouel and then he went for a year in Salt Lake City and then came back and worked at CEPH in the laboratory of Dausset. So Marc Lathrop went to Oxford but his love for France was very great and he returned and now he has a big laboratory in Evry near Paris.

PSH. So can I ask then, in thinking about the evolution of mathematical genetics, genetic epidemiology in France, because this is not really a field of mine, would it be fair to say the original person was Malécot and then there were influences on your group?

JF. Not exactly. The field of Malécot, was mathematical genetics and

theoretical population genetics. He studied immigration and consanguinity. I think what is called now genetic epidemiology began in the sixties at Jean Frézal's laboratory. We introduced the methods of Cedric Carter. So Cedric Carter was at the origin of genetic epidemiology.

PSH. That's interesting. But I get the sense that when Maurice Lamy, Jean Frézal, de Grouchy, Pierre Maroteaux, when they began, none of them had expertise in genetic epidemiology.

JF. No.

PSH. And so it was when you joined this group that that began. Did you visit Cedric Carter in London?

JF. Yes, many times.

PSH. And did he visit Necker?

JF. No to my knowledge, no but we saw him at Great Ormond Street.

PSH. Yes because he had a very big influence on genetics in Britain, also on human genetics and medical genetics. It was very sad that he died rather young.

JF. What also had influence, an in-depth influence, was the course that I had in the faculty of science. The book of Falconer had a very great importance.

PSH. Did you visit Falconer in Edinburgh at all?

JF. No but Catherine Bonaiti, I think visited him...

PSH. Sadly Falconer died one year ago and I was hoping to interview him, but I was too late. So during this time were you also doing work either in paediatrics or in clinical genetics, genetic counselling or . . .?

JF. I did some medical counselling but not much, I did from time to time and I began really to do genetic counselling when at the hospital of Salpêtrière they had decided to make a unit for genetic counselling on Huntington's disease. I did some clinical genetics at another hospital St Vincent de Paul in neurogenetics so they asked me to come.

PSH. Which hospital was this?

JF. St Vincent de Paul.

PSH. St Vincent de Paul, near Cochin.

JF. It's a children's hospital, a very old children's hospital. It was called before 'Enfants Assistés'. It was very interesting from an historic point of view. Napoleon had decided you can abandon your child at birth. There was a small box. The mother put the child

PSH. In the box?

JF. and some religious woman can take the child.

PSH. Good heavens. And until what year did this continue?

JF. I don't know but it was called Enfants Assistés. For children without parents.

PSH. But this was not still continuing when you were there?

JF. No!

PSH. Tell me who at the time when you started that collaboration, who were the main neurologists involved then at Salpêtrière.

JF. It was Yves Agid and then very rapidly Alexandre Durr and Alexis Brice.

PSH. I was wondering if there was someone from the previous generation of workers who was involved before Yves Agid?

JF. No. When I was a young student I was for 6 months in Salpêtrière and in Salpêtrière genetics was not known.

PSH. Really. That's surprising considering the tradition of genetic neurological disorders from that hospital. That's amazing.

JF. Yes. The first to really introduce genetics in this hospital was Yves Agid. He was not a geneticist but asked Alexis Brice to learn genetics, asked me to come and asked Alexandre Durr too.

PSH. That's very interesting. So that began your connection with Huntington's and similar things.

JF. Yes.

PSH. Now I think I am right that as well as the genetic counselling you have done a number of collaborative studies with that group also.

JF. Yes, I have some papers on epilepsy and some on Charcot Marie Tooth

disease, because I am working now with the molecular geneticist of this group.

PSH. Just remind me who that is. The name of that molecular geneticist.

JF. There is Alexis Brice, and Eric Leguern.

PSH. Ah yes. Tell me a bit about Réunion and your work on the muscular dystrophy there. Was this something which involved you directly or was it just in analysis of the data?

JF. Not, directly, but indirectly very much because at this period, the Director of Inserm was Phillippe Lazar.

PSH. Phillippe Lazar.

JF. Yes he was an epidemiologist and he asked me with other people to develop studies in the French departments overseas. The reason why we made some research in the French West Indies. Then I went to La Réunion. At Réunion we did many studies. I was not permanent there but I went to see them two or three times a year. But for muscular dystrophy it was Fardeau.

PSH. Michel Fardeau.

JF. He made all the clinical studies. There were some people from Inserm in La Réunion. We took blood samples and so we had for all the families, the lymphocytes and then I saw Bernard Barataud and I told him we have all the data. You have the markers. So for muscular disease, for you it is important to make this linkage study.

PSH. Yes.

JF. And this study was made at the markers level by J.Beckman and in three months, he did not find the gene, but the location was made on chromosome 16. So this was possible because I knew all the people working on this field in La Réunion.

PSH. Of course Bernard Barataud, he was in charge of AFM?

JF. Yes.

PSH. AFM had a very big influence on human genetics in France.

JF. So yes, this was when Barataud made his second téléthon. He had so much money that he was afraid.



PSH. I remember.

JF. And Daniel Cohen called me and said go and see Barataud and tell him there are so many diseases, hereditary disease to study, he needn't

PSH. He needn't worry.

JF. You can have much money.

PSH. That was a very fortunate occurrence.

JF. So they sent back and Daniel Cohen who had the first markers and this was applied for the first time on Réunion for muscular dystrophy.

PSH. So over the years you must have interacted with very many clinical geneticists who wished to have analyses made on their data.

JF. Yes, you see my last paper, it's a collaboration with many people.

PSH. Many people.

JF. Many people and different diseases because they asked me to do some statistical analysis, which I can do because I have no computer now. But you can see that I work with these people here also. I work a little with Stanislas Lyonnet and Jeanne Amiel.

PSH. I saw these collaborations are very many. Is there one which strikes you as being particularly productive among the many which you have done?

JF. I think the most interesting work is on Hirschsprung disease, because Hirschsprung disease is between a Mendelian disease and polyfactorial disease. So I think it is very interesting.

PSH. I'm sure you are right. And one of the rather few diseases like this, which is something perhaps unexpected. That's very very interesting. In terms of who now in France is continuing the statistical genetics work, are there many people continuing this kind of work?

JF. So there is in this university Laurent Abel who is working on some statistical theory.

The most important group is Françoise Clerget, Catherine Bonaiti, L. Abel, M. Lathrop and F. Demulais. These are the two main groups working on genetic epidemiology. They do studies, field studies, but also some theoretical work in this field.

PSH. Because the field of genetic epidemiology has always been a very small one across the world.

JF. Yes, very small, and now I am writing a paper "Multifactorial disease, a nightmare for the geneticist." (J. Neel wrote a paper "Diabetes a nightmare for the geneticist").

PSH. Yes, I think Neel's words are still quite true.

JF. There are many studies have shown that there is a problem. People don't find the same region, the same gene, and I was involved in a study on autistic syndromes. Now we know that there are many diseases, it is not one disease, but classical genetic analysis with non parametric methods have found some region. With many different diseases they find regions very difficult to explain but no gene. So I think there is a big problem in genetic epidemiology. I write this but many people said that genetic heterogeneity must be as big as for Mendelian disease. So what we call a disease is perhaps two, three or four different ones.

PSH. It does make things very difficult. Have you ever written a historical review of the development of this field in France?

JF. No.

PSH. You should do this now that you, in theory, have more time, because no one else I think could do this properly.

JF. Yes. The problem with retiring is there are many papers; I don't know where to put them. This is a big problem. I had very many archives but I have no places to put them and nobody wants them.

PSH. That is sad. This is one of the reasons why I am here.

Looking back over your work, would you say there is one particular person you could name who was a special influence in the development of your work and career.

JF. I would say two persons, Cedric Carter and Falconer, by his book and his papers.

PSH. The other thing I have been asking everybody who I see is, is there one particular piece of work which looking back, gives you greatest pleasure among the different things you have done? Either gives you greatest pleasure or you feel was a particular special contribution of yours. Is there one which stands out do you think?

JF. It was, I would say, the paper that you took, that was written with Saddi

on haemochromatosis. It was at this period here in France they said it was dominant, and we said it is recessive. But here it was a real big problem when we wrote this, it was not Frézal, Frézal admitted this directly. He said you are right, but many people said we were wrong when we were right.

PSH. That paper made very big changes in the way people looked at the disease.

I have one final question Josué, which may be a difficult one for you. I mean you have lived through the time of the consequences of eugenics and France had a difficult, maybe rather ambiguous attitude with not just eugenics, but I suppose with the Vichy regime and its attitude. Now as somebody growing up in the shadow of that and as somebody who I presume has a Jewish background?

JF. Yes.

PSH. How has this affected your thoughts on the development of human and medical genetics?

JF. I would say that I would show you what I show you before, the poster. [on eugenics]

PSH. Yes.

JF. Yes. Very interesting because on the wrong hypothesis there was not a scientific basis of eugenics in France before Vichy. There was no basis and there was no genetics in the school of medicine, no genetics in the faculty of science, and then Vichy came, and Vichy made eugenics. I wrote the first paper about eugenics, because some people criticise Andre Boué, who introduced prenatal diagnosis in France and there were many problems with Lejeune.

PSH. I can imagine.

JF. And was always the first to send them even prenatal diagnosis in most cases is dysgenic and I took a paper and, you know George Fraser?

PSH. Yes, I have interviewed George Fraser.

JF. George Fraser made a very interesting paper. When he showed that most of medical interventions, are dysgenic, not eugenic. Yes and I spoke on this subject in a scientific meeting called 'Club Européen de Conseil Genetique, in Lyon.

PSH. Yes I remember.

JF. And I showed them that medical genetics in most cases is dysgenic, not

eugenic. This was very interesting and then I wrote on this subject some papers, in French newspapers. And then there was Mattei that you know put in his Law on Bioethics that eugenics is forbidden in France. And there is I think a problem now, because when you do prenatal diagnosis for Trisomy 21, some say this is eugenics. I say you have perhaps a moral problem, but it is neither eugenic or dysgenic. And now this is the main problem. There is some confusion between the genetic basis of eugenics and what the people call eugenics.

PSH. That's true.

JF. So there are many problems. Many people say that you do eugenics. I say no. You can say that some prenatal diagnosis have a moral problem, but not really eugenics and there are many discussions in this field in France.

PSH. Do you think that it is more of an area of debate in France than in other countries, or do you think it is much the same?

JF. I think it's the same.

PSH. Are there other things, Josué, that you would like to tell me about, either your work or the field as it has developed in France, that I have not mentioned. Because I am aware that my knowledge of things in France is really rather limited.

JF. There is a big problem in France from the theoretical point of view, it's important. The first professor of genetics in France was Boris Ephrussi in 1946, around this year. It was not the university that asked him to be a professor of genetics. The Ministry of Education had decided that in Paris the university must have this. And then in the field of medical genetics Robert Debré, Lamy have developed this field. It did not come from the university spontaneously. There is no department of genetics in Necker-Enfants Malades, where they have very good geneticists. [Now there is a department, 2010].

PSH Is it not the case that Arnold [Munnich] and before that Jean Frézal, was it not a separate department then?

JF. No, I think Arnold wanted to have a department of genetics

PSH. I thought already it was. That's interesting.

JF. And you must ask him exactly

PSH. I will.

JF. But you see Salpêtrière have created a department of genetics. This is

quite a revolution because when I was a student in Salpêtrière there was a very great neurologist called Raymond Garcin said when you have two cases of multiple sclerosis in a family it's not multiple sclerosis.

PSH. Yes.

JF. So I think it is very difficult, even at Salpêtrière it's a department of genetics at the hospital level but not at the university level.

PSH. So there is a weakness in the academic foundations too.

JF. Yes a very great weakness in the academic level.

PSH. To finish, may I just ask about developments outside Paris. We mentioned Jean Robert. Now am I right, he was also a paediatrician?

JF. No he was a neurologist.

PSH. He was a neurologist. And his Unit. I knew him just a little only. Was his completely a hospital unit or was there an academic part?

JF. No it was a hospital unit of genetic counselling and then he became professor of genetics.

PSH. In the university or still in the hospital service?

JF. It was a mix. It was a university hospital.

PSH. And who has continued that work in Lyon?

JF. It is Henri Plauchu. Now they have more geneticists and they are doing much research. But the great department of genetics outside Paris is Marseille.

PSH. I am aware of one or two of the people who have been in Marseille but who founded the development?

JF. I would say, there are many people but really the founder was Mattei because he was a

PSH. This is Jean François Mattei?

PSH. Jean François Mattei, and what was important, his wife was a geneticist. She is not a physician but she is a very good cytogeneticist.

PSH. And Mattei himself, he was medical?

JF. He was medical. He was a paediatrician like I was and he developed much genetics in Marseille. Now they have a good research unit of INSERM.

PSH. Am I right that he was especially involved with some of the developments of congenital malformations?

JF. Yes like all the paediatricians involved in genetics.

PSH. And did Segolène Aymé do her training there?

JF. No. Segolène Aymé had begun her training in Paris and then went to Marseille and worked at the research unit and then came back to Paris.

PSH. So then there's Marseille, I was interested to read in the paper that Simone Gilgenkrantz wrote about Nancy and of course that was where Cuénot worked. But this was long before anything medical I think.

JF. It was Cuénot made I think very interesting work at the beginning of the 20<sup>th</sup> century. He had shown that in mice Mendelian inheritance was also correct but after Cuénot there was nothing.

PSH. That is interesting. So it seems to me that the history of genetics generally in France is really rather different from other countries.

JF. Yes. You can read in the book of François Jacob, when Monod had passed his PhD thesis in Sorbonne, the jury said "It is very interesting but genetics is not our problem".

PSH. Well Josué, thank you very much indeed, that is very valuable and if you think of anything else. . .

JF. I will write you.

PSH. And I think from the amount that I still have to do I will be coming back here, possibly interviewing. Well many thanks. I will now turn the machine off.