Ségolène Aymé

14 October 2011

I = Interviewer

A = Aymé

I **It's Friday 14th October 2011 and I'm talking with Professor Ségolène Aymé from Paris, and the interview is being made at the International Human Genetics Congress in Montreal. Ségolène, may I start at the beginning and ask where were you born, and when, if that's allowed?**

A Of course it is allowed. I was born in Paris in 1946 and I was certainly not in a family which predisposed me to become a scientist. I was educated to be a good housewife in a boarding school where we had no exposure to science, physics, mathematics; just nature, and we had training about how to hold a house and how to be a good wife and organise dinners and things like that.

I **What about your father? Was he, or any of your family, were they either medical or scientific at all?**

A My father was a publisher and he had a printing house as well, and my mother was a nurse. I think that the genes in science come from my great grandfather and great great grandfather and they are the ones who established the classification of butterflies and of coleopterans. They were correspondents of the British Museum. As they were very wealthy as publishers, and holders of the biggest printing house in France at that time, they were able to spent a lot of money for collecting butterflies and coleopterans. They made deals with priests who were going to Africa or Asia or South America: they would support financially their travel and staying there for 2 years and in return they would send butterflies and coleopterans from the country during 2 years. That is how that started.

I **I'm sure that must have been an influence on you.**

A I'm sure. It impressed me as a child and I always thought I had to be worthy of them.

I **Did you grow up with a love of natural history and plants, animals, things like that, or was it more as books?**

A No, it was more in books, but you know we had these boxes of butterflies and coleopterans on the walls, you know, and I knew they had collected 30,000 boxes and organised the classification. This was very intriguing to me. I can say that I have really a brain which is [laughs] designed for that type of activity as well. I did the same thing with syndromes.

I **Exactly.**

A - It's the same approach, and I have always been interested by that.

I **That’s fascinating. So you say that in your schooling you really had no science or -**

A Not at all. During my secondary school the teachers always said that I was quite gifted in literature, in Latin, so I thought it was true and that I couldn’t study science at all. Incidentally, when I graduated, I read a book about human biology and its logics, and I discovered a complex world that I totally ignored. I couldn’t understand the world if I was not investigating that part. So I decided straight away to go to science.

I **Was that the book of Jacob?**

A [laughs] No, no, no; it was a book by Alexis Carrel.

I **Oh yes.**

A And when I think that this is the book that influenced me, it’s unbelievable, but it is the truth.

I **That’s interesting. So when you went to university, what subjects did you take for your degree?**

A In fact I went to the Faculty of Science and I asked for the easiest class I could attend, because I graduated in literature and philosophy and not in science. The lady at the place where we were paying to go to the university, said, “The easiest is the preparatory certificate for medical school.” [laughs] So, I started with physics, biology and chemistry, and also embryology. It was the disciplin that convinced me that I wanted to go further for sure.

I **I’m amazed they let you into medical school with not having done anything before.**

A At that time, it was possible, not any more. I think, finally, that the fact that I was trained in literature and Latin has helped me a lot when I started to get involved in policy development.

I **Which medical school in Paris did you go to?**

A When I started in 1963, there was only one: the University of Paris. It divided in 10 universities in 1968 when I was at fourth year; and then I was at Bichat-Beaujon University.

I **So did you do most of your clinical studies then at Bichat-Beaujon?**

A Yes, but also at Necker, Cochin, Saint Vincent de Paul. Very quickly, I was very disappointed by the medical studies; they were very empirical; very little logic. The teaching was not good. Suddenly I understood what I needed to be exposed to more Science. We were in 1968. In May the revolution started and I was one of the leaders at the Faculty of Medicine. I learned really everything in politics in a few weeks time. It’s strange how quickly how you can get to understand better or differently the world, just by chance, It happened at the right moment for me. I was nominated as representative of students in charge of liaising with the researchers and the researchers had nominated someone to be the one to link with the students. I met with this guy and this guy was Philippe Lazar who become after the Director General of INSERM in 1982. He was a top statistician and mathematician, in France that means a lot. So, I decided to study statistics applied to medicine because of this meeting with Philippe Lazar. We are still in contact over 40 years later That was the best thing I could have decided because it was totally new to me, and it was a new opening also on how to look at events in biology and medicine. I did a master, doing my medical studies concurrently. Then I decided to have another vision of biology and to do a master in genetics in parallel with my medical studies. I was so happy to study at the Faculty of Science, with excellent teachers such as Piotr Slonimsky. I loved that so much. During that master, I studied ecology because I wanted to have even a broader view of biology. It has been hard for me to stop studying once; it was so pleasant; so pleasant. During that time, I did my residency mainly in labs in virology, bacteriology and then cytogenetics, as it was for me a proxy for science; I did little clinics.

I **So had you already by this stage decided to make paediatrics your main clinical area?**

A Not at all. I was driven only by curiosity. I had no idea of what I could do. I was just discovering the world that has been hidden to me during so many years. In addition, I had no idea of my value and no idea of what I could do with my life. Many things happen just by chance. In fact, I was offered a permanent position in virology in Paris when I was only 25, but it was a time when I had just married and I had my first son, and life in Paris was not pleasant for a baby. We decided with my husband to apply for a position in the south of France where life is much easier. I applied for a position in virology because it’s what I knew best. It’s because of my experience in virology that I met with Andre Boue, as he was a virologist as well. This experience was very useful because I learned how to culture cells which helped me after when I started to develop prenatal diagnosis... So I applied in the south of France and I did not get any response from the virology labs. As I had a master in genetics, I tried the labs of embryology, cytogenetics and I got an answer from Marseilles from a guy who had just opened a laboratory of embryology-cytogenetics, who said yes without seeing me. At that time, it was so easy to get a position. We moved for September and I discovered that the guy was not interested in really working. He was nominated as head of this new department because he had been very influential in maintaining the students very quiet during the ’68 [laughter]. I was very disappointed and I started to look around in Marseilles where I could do real work. After a few days, I met the head of paediatrics who wanted to develop genetics from scratch. He accepted me immediately, knowing that my salary was paid already by another department !

I **Who was the head of paediatrics in Marseilles?**

A At that time, his name was René Bernard. The one who wanted to develop medical genetics was his young assistant, Francis Giraud, who became my boss. Francis Giraud had already a very small lab of cytogenetics with two technicians; Jean-François Mattei was working in the department, and his wife, Marie-Geneviève, was working as a technician but not employed officially. She was working as a volunteer to develop staining of chromosomes. Both of them formed a young couple, charming and bright; She was a housewife giving a few hours a day to this cytogenetics lab.

It’s where I started also as a cytogeneticist also involved in the clinics. It was a big shock because I was not prepared at all to face patients with unknown diseases to me; we had no books, no training; it was a very shocking experience.

I Were these genetics clinics or paediatric clinics?

A These were genetics clinics but we were in a children’s hospital so it was mainly only children coming essentially for cytogenetic analysis. At that time, malformation or any genetic condition would have a chromosomal analysis. That was the only thing to investigate the genetic basis of diseases.

I Was it Jean-François Mattei who had started these clinics?

A Yes, I am not sure. But the idea came from René Bernard who was a very, let’s say, thoughtful man and he wanted his young assistants to develop sub-specialties.   He had chosen Francis Giraud for genetics. We were in ‘72. There was the plan to open a new university hospital in the centre of Marseille, La Timone, with a building for 700 beds in paediatrics. We had the opportunity to design a true department of medical genetics in this hospital, and that was really, for me, a magic opportunity to decide on what would be the future of this discipline based on the needs. We settled in ‘74 in the new building where I spent 20 years. It was the first real centre of human genetics in France, offering in the same place clinical services and cytogenetic services. In Paris, the clinic in Necker Hospital was not linked to any lab. It was really the concept of medicine and biology linking to develop better services. It developed quickly as it was easy to get funding from local and regional health and research authorities.

I You could do it as well as they did it in Paris.

A Exactly. So it was very happy days in the sense that we had the feeling that we were really developing services for people at needs. My experience in cell culture was very useful for developing prenatal diagnosis in ’75. When I heard that Andre and Joëlle Boué had started to culture amniotic cells, I went for one day to see Joelle. She just showed me how she was doing and I started in Marseille with a colleague in obstetrics who was open-minded. But this created a tension in the team. Giraud, but mainly Jean-François and Marie-Geneviève Mattei, were opposed to abortion and they thought that it was not ethical to develop prenatal diagnosis. I was asked to stop this activity or to do it outside the human genetics centre. So, I negotiated with the virology lab, where I knew the people, and they let me start the activity in their lab; they gave an incubator. I developed the activity there during several years, bringing the plates when the chromosomes were ready, to the genetics lab. It was a very strange situation.

I Was that the time, I heard from talking with Joëlle and André Boué and also from Simone Gilgenkrantz that there was a big division in Paris, and perhaps the whole of France, because of Lejeune’s views and…

A Exactly; and Jean-François Mattei was very close to Lejeune; he had been trained by him. So I would say the people from the left wing were with Boué, and the right wing with Lejeune: two schools and two political orientations. But it did not last very long.

I think it lasted until 79. In 79 prenatal diagnosis became very fashionable, it was a new and valuable service covered by magazines. We had a lot of requests, the clinics were full of women coming for that new service. So, at the end of 79, suddenly Giraud and Mattei told me that the activity would be incorporated in the genetics lab and that somebody else would take over from me. Jean- François took the activity to get some independence from Giraud, despite his ethical stand. It has been painful for me. To recover, I decided to take a sabbatical somewhere. I moved to Montreal and started work at McGill, at the children's hospital, just to have a positive change and think about my future, find out what I wanted to do next.

I **Before we leave Marseille, can I ask: in the new department which had been organised, apart from clinical genetics and cytogenetics, were there other laboratories like biochemical genetics or anything of that kind?**

A No. For biochemical genetics, we collaborated with Lyon.

I **And was it a hospital department or an academic department?**

A Hospital department.

I **Right. And did you, or were there links between yourself and the Matteis and any other geneticists either in biology or in the university? Or was it very much hospital based and orientated?**

A It was totally hospital based. Now I realise now that's strange? That's very strange. But this hospital department became quickly an INSERM unit with a lot of research grants. Giraud was head of the INSERM unit, Mattei had a research team and I had mine as well. This happened because I switch from my position of assistant professor to a position of researcher at INSERM in 1978. I had to do that because my position was withdrawn at the time where I was about to become associate professor. It was to give it to the new wife of the professor who hired me at the beginning without giving me any work to do. The only possibility to continue working there was to appiy to become researcher at INSERM. I was lucky enough to be hired. This negative experience turned to be a positive one, because INSERM is a research institution where you are evaluated, assessed, only through your work and publications, not who was your father and who is your boss.

I **Okay. And at that time you say that really there ods no other fully developed medical genetic units or centres in -**

A My view is that in Europe there were really Leuven and Marseilles. For me these were the two centres that were really comprehensive in terms of services to the patients and optimal exploitation of patient data for research purpose. I had developed a lot the informatics. The files were computerized in 1978. When I left, the department had 23,000 family records, fully exploitable. At that time, it was very unusual. I had also organized a biobank of cell lines from patients with unknown syndromes. I developed a system to support the diagnosis of rare cases, called Gendiag, which was up and running in 1974, the ancestor of Orphanet. On I also set up a registry of malformations covering birth defects from children born in the department of Bouches-du-Rhône around Marseille, to have data on families seeking advice or not. We were very well organised.

I **I saw looking through your publications that at a very early stage you had written on computerisation of records and that also there was an interest not just in malformations but in some of the epidemiological aspects -**

A My research activities were in epidemiology and public health around the adoption of new technologies and practices in genetics and the use of computerised methods to delineate syndromes. I always stay away of the activities developed in Mattei’ s team to avoid potential conflicts, except when he asked me to join a project.

I **So your interest and work in this field really goes back to the very beginning.**

A Yes, absolutely. And you know I was in fact very complementary to the Matteis because Marie-Geneviève Mattei was highly skilled technically. She was extremely handy in cytogenetics; and Jean-François was very, very clever; she was a good technician; and he had a broad view: a perfect match. But I was the one who had the brain more formatted for statistics and Biocomputing. I was a very good organiser and manager when both of them were not so interested in that. I like to make people happy, and I like to establish collaborations. The department was pretty good but we could have done better with more cooperation.

For me it was a very hard time, May be because I am a woman. I was not at all recognized for what I could bring. My stay in Montreal, at McGill, opened my eyes on the unfairness of my situation in Marseilles. The department of human genetics at the Children’s hospital was an excellent department, with very open people like Charles Scriver and Clarke Fraser. Suddenly I saw in their eyes that I had some value. I was even offered the position of Clarke Fraser who was about to retire, that I declined as life in Montreal could not compare with life in the south of France. I really gained confidence and decided to build something on my own.

I **How long were you in Montreal?**

A Just one year. But after that I came as a professor for the summer time during a few years. It was like a decisive year, Sometimes somebody changes your life like Clarke Fraser. He took me to American meetings. I was the first European accepted in the David Smith group. It was the start of an international life. International connections were very decisive for me and still are.

I **It must have been difficult moving like that with your family?**

A Yes. When I moved to Montreal, I had already divorced. I was a single mother with two children. It was not that easy but I managed. [laughter].

I **What were the main things that you learnt during your time in Montreal with Clarke Fraser and all the others?**

A I learned first the culture of working as a team because in Europe the dominant model was the patron and the pupils, and in Montreal it was totally informal. We had a journal club where the youngest student could express ideas; and also the fact that

I could go and get advice from anybody at McGill, without any appointment. The doors were open. What impressed me the most was that I arrived on a Monday, on Friday Clarke Fraser asked me whether I wanted to do some research on my own. I said, "Yes, I would like very much." He said, "Could you give me two pages by Monday or Tuesday?" "Sure, I will." And I got the money the week after. That was the power of McGill. It was a rich university, with their own money they could spend, and decide on. That was very impressive. It was the North American spirit to let young people have a chance to show what their capacity. That was very different from my experience in France where the hierarchy is so heavy. That was the first aspect. A second aspect is that I discovered that biochemical genetics also was a very important part of genetics, and the fact also that in research if you want to do something really creative you have to link with other specialities. I did a study on natural selection of embryos with trisomy 21, and I discussed a lot with people from the mathematics department at McGill. I would never have done that in France because I would not have had the idea to go and see people who were not in my discipline. Every time that I was discussing with Clarke he was saying "Go and see this one" or "Go and see that one". It was really magic for me.

I Were you already an INSERM employee when you went to Montreal?

A Yes, and I came with my salary from INSERM which was a disaster because at that time the franc went down [laughter] and the dollar went up. [laughs]

I It always happens that way round. It never happens to anybody the other way round! Yeah, and so did you have a post to return to then, or did you go back to Marseille initially?

A It seems silly but at INSERM, it's still the case, when you have a position it's a permanent position and you own it, which means that you just have to say where you want to work and that is it; you go with your position wherever you want, not longer than 5 years abroad.

I That's a wonderful thing.

I So when you went back to Marseille, I mean, what did you go back to?

A To the same department with my position. It was hard to even obtain an office. But finally, Giraud was clever enough as to understand that I was an asset for his department. He was not a scientist but he was good at finding money. He let me develop what I wanted. At the same time, Mattei decided to go into politics so I was left with the management of the department, without the position, as I was a researcher. But I acted as a medical geneticist in addition, during all these years.

I What year was it that Mattei moved to Paris? Am I right in that he became Minister of Health?

A Yes, in '81 when I returned from Montreal, we had for the first time a socialist president. Mattei was very much a right wing person. It was like a big shock to him and to many people in France. I was delighted. He decided at that time to go into politics; he started to be elected as mayor of an area in Marseille that had always been communist. His capacity to take over this area impressed many people. But he had in mind, from the beginning, to become Minister of Health. He became quite influential in the right wing party in France and was elected as a deputy. Finally, he was the one who wrote the Bioethics law that we adopted in 94. It was really a very significant contribution. It was clear that he was on the track to become Minister of Health and it happened. Unfortunately it did not last very long as he was sacked, because of a mistake he made in communication, when we had this heat wave during a summer which killed thousands of people. He was on his vacation in his house in the south, speaking to media from his swimming pool, when he should have returned to Paris.

I **Did he return to a medical career?**

A Yes. He had to. He returned to Marseille but never worked back as a clinician. He was head of the department of prenatal diagnosis [laughs].

I **Am I right that his wife continued to work in cytogenetics?**

A So his wife after a few years where she worked without any salary, finally got a position at the CNRS and after that she did a nice career in this field. She was very successful because she developed techniques that were highly cited. I believe they both continued to act in research as a couple; it's like the Boués, Joëlle and André. I think Jean-François and Marie-Geneviève were very complementary. Jean-François had more ideas and she was the one really working, and one without the other would not have been as successful.

I **Am I right that they are both still living -**

A Sure, yeah.

I **And in Marseille or now in Paris?**

A No, no, they are in Marseille. Their family is in Marseille. Marie-Geneviève just retired last year and Jean-François was given the position of President of the Red Cross in France, so now he comes to Paris quite often. Ironically the Red Cross Headquarters is in front of my building in Paris [laughs], so we share the same parking places.

I **What year was it that you moved to Paris?**

A I moved in 91 because I met my current husband. His job was in Paris and I had no choice but to move back there if I wanted to share his life. It was for me very painful to leave everything I had built up. I had to restart from scratch, which was not easy. I had to negotiate with the INSERM that I could create my own INSERM Unit. We were at the beginning of the human genome project. I wrote down a report on the assets of France in this race; my analysis was that we had a pretty good health care system, with a lot of patients deeply investigated. I thought that the clinical data and well diagnosed patients would be very important for the exercise, which proved true. I proposed to develop a service to match research teams with clinical teams and to find human material for the human genome project. This was accepted; it's how I re-started. It was a very small service but quickly people were happy with what we were developing; it was my main activity, trying to understand the needs of both sides. I developed a database of expert clinics and expert researcher, with their diseases of interest. This was another ancestor of Orphanet. In 95, I received a phone call from the Ministry of Health saying, “We are looking for someone to write a report on rare diseases; could you help?” I said, “I have no idea of rare diseases but all genetic diseases are rare”. I accepted the challenge and started to write this report with five or six colleagues. When I reported to the Minister of Health, the proposal was to develop a service to generate information on all diseases and publish them on a website. The concept of Orphanet was born. It was the merge of Gendiag, my database of rare syndromes to retrieve diagnoses; and of Geninfo, the database of expert services. I got the funding to develop that very quickly. We started in 96 and we opened the website in 97. The two ancestors were developed to serve the needs of researchers and clinicians. The website was conceived to serve the needs of healthcare professionals and patients.

I **So what now does your Orphanet team consist of?**

A My Orphanet team in Paris consists of 35 people.

I **That’s a lot.**

A Yeah, yeah, yeah. Plus about 30 other people in other countries. There is a team in charge of the inventory of diseases and of the classification, another annotating genes, another collecting epidemiological data. There is a team to develop the encyclopaedia; another one collecting review articles and clinical guidelines. The website is produced in English, then translated into French, German, Italian, Portuguese, Spanish and Dutch. There is another team that collects information on all the drugs which are developed for these diseases, we follow the products from the earliest stage of development, like in animal models, up to the marketing authorisation; and we have another team which is in charge of the information on expert clinics, clinical labs, patient organisations, registries, research projects, clinical trials, disease by disease. And now in 38 countries, so it’s a major enterprise. And then we have an informatics team and a communication team and we have a newsletter, an electronic newsletter, which has 15,000 readers and we publish also reports. Let’s say we present the data in a comprehensive way; we have a report on drugs in development; we have a report on the epidemiology of rare diseases; we have plenty of reports. So it’s a huge enterprise. I have also established a journal the *Orphanet Journal of Rare Diseases* to boost the publication of articles in this area.

I **Does most of the funding for your work come from the European Union? Or does it come mainly from INSERM and -**

A It’s a quarter INSERM, a quarter Ministry of Health of France, and the other half is mainly European Commission, grants from the European Commission. We have alsorevenues from companies using the data from the website for research purpose. The whole dataset is freely available for academic researchers.

I **Well, that’s pretty amazing.**

A Yeah, yeah, amazing.

I **If you look over the things you’ve done, is there any single particular piece of work or area of work which you feel is your special contribution? Which would you feel is the one that makes you most proud of all the things you’ve done over the years?**

A I think that my contribution is in designing the landscape of services in Europe, It started with my involvement in the activities of the ESHG after 1994. I chaired during 10 years the Public and Professional Policy Committee of the European Society of Human Genetics. We have produced many reports and recommendations on good practices from a public health point of view. This activity required to work with experts from many specialties and from many countries. I learned how to organise the interaction and how to make the most of it to produce a consensus. In my own country, I was very instrumental in shaping the organisation of prenatal diagnosis and serum marker screening. We developed good information to patients; quality criteria for labs, organise them and network them. We designed prenatal services which were equitable and efficient. I dedicated many years to that and I’m happy I did it as now it lasts. I think it has even more impact on the women and the babies than what I do with Orphanet. In 2004, I had the opportunity to impact on a new national law on Public Health. Among the 100 goals, 5 were chosen for a national action plan with funding. I succeeded in making rare diseases one of the 5.The French national plan is still a model for other countries. After that, I was nominated as chair of the Rare Disease task force, then of the EU committee of experts on rare diseases. We developed an analysis of the problems that could be overcome by action at country level or at EU level. In some years, all the European countries adopted a plan or a strategy and the EC took action in many fields. I am very satisfied to have impulsed these initiatives, even if I know that the success was due to a positive conjunction of other factors as well. I’m also proud of Orphanet because I think that it illustrates the approach I try to have all my life long: to use new knowledge and new technical possibilties for the benefit of patients. I like fixing problems.

I **One question, just to finish, which I’ve been asking to everybody is: is there any particular person that has been a special influence on your career, that stands out, or do you think you’ve very largely made it yourself?**

A No, no, no. I certainly did not make it by myself. I was influenced by Andre Boué, who knew what he wanted to do in the field of prenatal diagnosis, despite the difficulties and obstacles. He did his way, and I think that was really an example. I was very much impressed of course by Clarke Fraser who was so modest and so imaginative and creative; but also by Hans Galjaard, because in fact, in the early days, the field of prenatal diagnosis was very much influenced by the biochemists, and he was the leading person. He had so much culture in science and medicine. He impressed me a lot. I thought he was really a fantastic guy. Margareta Mikkelsen was the one who supported me as a woman and involved me in the management of the Human Genetics Society. Finally Marcus Pembrey was my best colleague to discuss, science, medicine, philosophy and politics.

I **Ségolène, before we finish, is there anything that you’d like to say that you feel I should have covered but I haven’t at all?**

A [laughs] No. What I regret sometimes is that, because of all the difficulties I faced, I’ve not been able really to build a big department or a big team. I hope that the resources I have established, and the policies that I have fighted for, will remain useful to patients. To close where we started, my scientific life brought to me what I was looking for as a teenager: Understand better life, humans, work with clever colleagues, and take my share in the evolution of our complex society.

I Yes, well thank you very much. I shall stop the machine there and many thanks for your time.