Hans Galjaard

Personal Details

Name	Hans Galjaard
Dates	Born 8th April 1935
Place of Birth	Rotterdam, Netherlands
Main work places	Rotterdam
Principal field of work	Biochemical genetics of inherited metabolic disease

Short biography

After training in Medicine and Paediatrics, he undertook research in cell biology, focusing on inherited lysosomal disorders and developing techniques of prenatal diagnosis. In addition to founding medical genetics research in Rotterdam, he was largely responsible for the development and health service funding of a network of medical genetics centres across Netherlands and has also been extensively involved with ethical issues in human genetics and communication of science to the wider public.

Interview

Recorded interview made	Yes
Interviewer	Peter Harper
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INTERVIEW WITH PROFESSOR HANS GALJAARD, 09/12/2010

I = Interviewer (Peter Harper)

G = Hans Galjaard

I Today is Thursday, December 9th, 2010 and I'm talking with Professor Hans Galjaard at his home in Rotterdam. Hans, just to begin, can I ask when and where were you born and brought up?

G I was born April 8th 1935 in Leiden, which is an old university town in between Amsterdam and Rotterdam. And I've lived there my whole youth, and I also studied medicine there; so I stayed there up till my PhD and my medical degree.

I Can I ask, were your parents or any of your family either medical or scientific in some way?

G No, relatively simple people. And although my father was a very good chess player, and my mother played violin, they were very simple. And I was the first to study medicine in the family.

I What was it that brought you into medicine?

G Well, I had two brothers, I was the eldest, and then in '42, so 7 years after my birth a second boy was born. And after about, everything seemed to be normal and then when he was 6 and started to go to primary school, some parents of children with whom he played started to complain to my parents that my brother was so aggressive. And gradually this became worse and he was very difficult to handle at home and he had to go to a special school so he couldn't be maintained in a normal primary school, and finally he went to neurology and came up into an institution for the handicapped. And they didn't know exactly the diagnosis but later, when I studied medicine, I could see his medical records when I was doing clinical work at this neurology department, and I saw that the professor at that time already predicted that he would go down and down in terms of mental retardation, and also become blind. And this is what happened. He died when he was 18 and he never had developed very well also physically, so he was still small, and was in a wheelchair. This impressed me very much, and also my parents of course; he died one week before my wife and I married, and I will never forget that. I think that this deterioration of a life and not knowing the cause made me to study medicine.

I Yes.

G And I discovered later on what the disease was. I wrote a book in 1980 called Genetic Metabolic Disease, a big book, and I was retiring for that in our little holiday home in the middle of the country, and I was sitting by myself with a pile of papers for every metabolic disease I wrote about. And at a certain moment I saw an American paper I think, and there were pictures of a disease which was metachromatic leukodystrophy and I saw a picture and I thought, "My God; this is my brother." It was another patient but it was exactly the same. So then I discovered that it was a juvenile form of metachromatic leukodystrophy. It was impressive; the second moment to be impressive.

I Yes, this must have had a very powerful effect.

G Yeah.

I After you'd gone through medicine, did you go straight away into the laboratory side for research, or did you first go to paediatrics or some other clinical discipline?

G No, even before I finished my medical clinical degree, I went into a laboratory, not because I

was so scientifically interested but because I wanted to earn some money, and there was a vacancy for a student assistant in an institute for rheumatoid arthritis in Leiden, and I took that job and became interested in laboratory research. I had a very tough boss; a Hungarian, very artistic histologist, Dr. Janos Szirmai. Very old fashioned, and very hierarchical, and he repeatedly told me that I was an absolutely useless person but that I was an attractive man for women so he advised me to be an obstetrician gynaecologist, and stop research. And finally I stayed with him for 4 years and I got a cum laude PhD in his lab on a thesis that had to do with ageing of cartilage.

I I saw, actually, in your publication list, your first papers were on histochemistry of cartilage. I'd been wondering how that originated. Now after your PhD where did you go next? Or what did you do next?

G After my PhD and medical degree I had to go into military service, first to Germany because it was the cold war at that time. And most of our armies were in Germany, not in the Netherlands. I was a medical doctor for a part of the tank troops; then the cold war became so serious that the government got afraid of atomic bombs. They realised that in the Dutch army there was no knowledge about the medical effects of atomic bombs. They selected me, because I'd done a PhD, which was an exception for young medical doctors in the service; and they selected me to be trained in radiobiology and sent me to England, to Harwell. I stayed there for a while and then in another lab here in the Netherlands, the Medical Biological Laboratory of the National Defence Organisation. That was the first real research I went to do on my own, because I was asked to study the effects of radiation on intestinal epithelium.

I Now at that time, Harwell was the home of some very famous geneticists also: how much contact did you have with any of them?

G No personal contacts, but as a teacher. We were with a group of about 12 people from different countries; basically the countries that later on got the atomic bomb. [laughs] Israel, for instance. And also a radiologist from Spain and Holland has of course no atomic bombs. As teachers I remember John Evans for instance, and also Mary Lyon was there. I was impressed by, although the time was short, the overall high quality. There were two major differences with my own country at that time. The one was the higher quality of teaching than I was used here; the second is, we have quite a separation between a person who is doing research, and a person who teaches. And usually in our country the priority is on science: you have to publish, you have to show that you are good, that you're better than the others, and the students, sorry for them, that's basically for the people who are not so gifted in research. I found that much better in England. There were people there, including later on also Nobel Prize winners who were quite willing to talk to first year students, and take questions, and take them seriously in their questions. So you have, in that sense a very good tradition in the UK. I've always remained a fan of the UK in that respect.

I I know that. I know that. Now how long were you at Harwell altogether?

G Four months. And then I went back to the National Defence Lab here.

I Yes. May I ask was that in Leiden, or -

G No, that lab was in Rijswijk. It's near The Hague, and it was a huge multidisciplinary laboratory and they were pioneers in our country in E coli molecular biology; they had a radiation department; they had a biological warfare department and one on chemical warfare. I was in the radiation group, as I said and I was asked to study the effect of radiation on intestinal epithelium. Initially I used histochemical methods, but realised that this was too qualitative. I then started to develop quantitative microchemical methods combining 2 types of approaches. One developed by Oliver Lowry in the United States, who used ultramicrochemical analysis for certain enzymes in single nerve cells and I extended that to a

broader array of enzymes. And then I was stuck because I could do chemical reactions in a very small volume but there was no way to measure the spectrometry or the fluorometry. Then I went to Caspersson in Karolinska, who was a very top guy in making use of microscopes as measuring instruments. There I made a concept to develop a new type of ultramicrochemistry for enzyme analysis in few or even one single cell(s). I built that here in my own lab later on and had contact for many years with Stockholm on that issue as well as with David Glick in Stanford. Later I used this method both in studies on intestine and in prenatal diagnosis and genetic complementation studies. From then on I got PhD students and foreign guests and my career went relatively fast.

I **Can I ask: in that early stage, am I right that you were working with Dirk Bootsma for a while? I saw that his name was also on some of the intestinal epithelium papers.**

G Yes. That is, for us it's very funny, both for Dirk and for me: we are still friends and have regular lunches together. We are both retired. Dirk was younger than I, only 2 years, but in research I was a few years ahead. I had already finished my thesis when I came to that laboratory, and he was also in military service. He's a biologist, I was a medical person, and he was also designated to the National Defense Organisation. He studied the cell cycle and the inhibition of the cell cycle under irradiation. We were in the same small group and we became friends very soon. In 1965 when I had worked there for about 2, 3 years, I was invited to take part in a new medical faculty in Rotterdam, and Dirk had yet to finish his PhD thesis. When I started in Rotterdam to build up a Cell Biology department under my former boss in Leiden, Szirmai. I realised that I would very much like to have Dirk with us. So I went to my boss and said, "I know a person who I think is a very gifted researcher, and his name is Dirk Bootsma. Can I introduce him to you?" And he was still in Leiden. So I went with Dirk to this Professor Szirmai who asked Dirk, "What are you doing?" And Dirk's answer was, "Well, I'm very much interested in fibroblast cell cultures." And the answer of Szirmai was, "That's a pity." And Bootsma was completely surprised, and said, "Why is it a pity?" "Well, you know, all important scientific questions are not in the cell but are in the substances between the cells."

I **[laughs]**

G And then I thought, "This is the end of my friendship with Dirk Bootsma" but he still decided to go Rotterdam, and two years later our boss got problems with the dean and went out. He retired. I succeeded him as a boss and the first thing I did was to ask Dirk to stay with me. I did not feel I was his boss, because I felt more like a friend. But he accepted that I would be the boss and after two years he was made a professor in genetics himself. We always stayed together; whatever happened to me or him; we always wanted to stay our departments close together.

I **When you became the director of this institute, was it an institute for the whole of cell biology, or was it specifically for genetics, or a combination?**

G Yes, it became quite a big department soon. I think 30, 40 people when I became the boss in '68 and it grew to several hundred in two, three decades. I had taken my microchemistry and my intestinal work with me to Rotterdam, and Dirk had taken his cell cycle work. Our boss was wise enough to listen to both of us, so Dirk built a big cell culture department; I built a big chemistry department and microscopy department. And later a third professor was nominated, his name is Otto Vos, and he was interested in radiobiology and immunology. Dirk and I fertilised each other very much. He knew a lot about DNA and I knew quite a bit about protein chemistry. Dirk introduced me to cell culture and I started prenatal diagnosis and combined this with my microchemistry. And then it became a boom because we could do prenatal diagnosis of metabolic disorders much earlier than other people, so I got samples from all over the world. That was around 1970. And Dirk started DNA repair and gene mapping with cell hybridization. Dirk found that two different gene mutations were involved

in patients with different clinical forms of Xeroderma Pigmentosum using cell hybridization and autoradiographic analysis of DNA synthesis. When I saw this procedure, I thought "Wait a moment; maybe we can extend such complementation studies to a variety of genetic enzyme deficiencies like Tay Sachs and some of the GM1 gangliosidoses. So we fused cells from patients with different clinical variants and used our single cell method to see whether the enzyme activity came back or not. And I will never forget, I went to London; I was very proud with our first paper in Nature and there was Pontecorvo in the audience. He had written a whole book on cell hybridisation for lower organisms. After my seminar, I think in the Cancer Research Institute Pontecorvo said, "Why are you so excited?" And I said, "Well, because…" "Yeah, did you not expect complementation because everywhere is complementation. So, why should human cells not complement?" [laughs] So Dirk and I have stimulated each other during our whole career in the department of Cell Biology and Genetics.

I **One of the things I noticed, looking at your publications was that things seemed to take off very suddenly and together both in terms of your publications on inherited metabolic disease and the prenatal diagnosis. It seems as if maybe at the first half of the seventies there was a rush of things to report. I mean, is that how it happened? Or was it a lot more gradual really?**

G Yeah, I think it was gradual. The work on prenatal diagnosis went relatively fast. My scientific interest was however focussed on the elucidation of genetic metabolic defects in unknown diseases, so to say. But prenatal diagnosis was very practical and got worldwide much public attention. Not only technical and clinical, but also ethical discussions: "is it right to abort a Down Syndrome baby" and that type of thing. Well, many pregnant women came to us because of increased risks of chromosomal aberrations, neural tube defects and metabolic disorders. And, as I said, we got samples from many, many countries including the US, because the law in most countries did not allow to abort after 24 weeks. For biochemical diagnosis they had to culture a long time; 6-8 weeks in the beginning. And we could diagnose some dozens of metabolic disorders in 10 to 14 days or even earlier. I've never travelled so much as at that time. I had to lecture everywhere. I saw, in a very short time, most parts of the world which I'd never dreamt of during my studies on intestinal epithelium which was of little practical importance. During my whole period in Rotterdam from 1966 - 2001 the main emphasis has been on delineating enzyme defects in lysosomal disorders and later the discovery of responsible gene defects in neurodegenerative disorders. This led among others to the discovery of a new protein, the protective protein, the finding of a new genetic mechanism in Fragile X syndrome and an alpha-glucosidase therapy for patients with Glycogenosis II.

I **Was there, in Rotterdam, before you and Dirk came, was there any tradition of human genetics as a specialty?**

G No there was nothing. There was no academic hospital. There was just a normal hospital with surgery, obstetrics; there was no genetics. And in fact I was not a geneticist either. Dirk was a geneticist but not a clinical geneticist; he is a biologist. At that time there was quite a hierarchy: there were the medical specialists, and the rest. And the rest was considered more or less as helpers, so they would say, "Can you project the slides for me, please?" And Dirk had a more difficult time than I. I was a medical doctor and because of the prenatal diagnosis I was more or less acknowledged as an important part of the hospital. If I just had studied the genetic variation of Tay Sachs disease or GM1 gangliosidosis, it would have taken a much longer time. Later, Dirk got more and more recognition, because people realised he was an internationally recognized scientist. One of our best. Yeah, in the beginning of our new medical faculty there was no genetics at all. We had to ask Marcello Siniscalco to come and do the teaching for the first year students.

I **He was then in Leiden?**

G Yeah, yeah. Charming man.

I What made you choose lysosomal disorders as a special field of interest, rather than some other metabolic groups?

G Yeah, maybe it was so close by? Because de Duve was not so far away and Hers discovered the first enzyme defect in lysosomal storage disorders; in Glycogenosis II. I worked together with the Brussels people because they sent me people at risk for Tay Sachs disease for prenatal diagnosis and glycogen storage disorders. I started to work on the diversity of lysosomal diseases. I didn't have great ideas at all. But then, I don't know why, but in a relatively short time, we became quite successful in this lysosomal field because the lipid people in America invited us, and people involved in biochemical diagnosis of metabolic diseases. The combination of the general interest in metabolic disorders and the rapid advances that were made in the US: Brady, Elizabeth Neufeld and our combined clinical, biochemical and genetic studies received international attention. Old fashioned good biochemical studies, together with new things like cell hybridization, complementation, a little bit of sensation of the ultra microchemistry, one single cell, that's nice; that made us, at that time, roll.

I How long did it take before you were able to build up an all round medical genetics centre, from the beginnings with more biochemical genetics?

G When I started in 68 with the first experiments on metabolic disorders, and did the first studies of alpha glucosidase and alpha galactosidase; I saw you interviewed Jan Mohr also. Is he dead? Because I saw a cross.

I Yes, Jan died last year.

G Ah, I didn't know. Well, I wrote one of my first papers with him on the prenatal diagnosis of Fabry's disease. When I started, at that time, end 60s beginning 70s, I realised that our basic research would be endangered if it took too many of our people to do genetic services. In the beginning it was not much but it became more and more. Then I wrote a report, I think, in 71 or 72, to the Ministry of Health, with a kind of prediction of how I thought genetics in medicine would grow, in general, because already there were chromosome studies, especially in England; France also. So I saw this, I saw the biochemistry myself, and DNA didn't exist. Counselling was just a hobby for a few paediatricians at that time; and not my hobby. But I realised it will become everybody's hobby because you must provide proper counselling after diagnostic laboratory work. So I wrote a nice paper with future predictions and didn't even get an answer from the Ministry. They didn't answer even that they received my paper. I talked about this to the Chairman of the Health Council; that's the highest advisory council we have here in this country. It still exists. And this man was very powerful. He was a professor of internal medicine in Leiden; his name is Haex. He listened to me, became very enthusiastic about the ideas and he went to the top of the Ministry and invited them to his room in Leiden, and invited me as well. An official advisory committee was formed in 1973, and I was the secretary of that committee. The next period I contacted experts in cytogenetics, biochemical diagnosis and various clinicians to prepare an outline of the needs of comprehensive clinical genetics centres attached to our 7 University Medical Centres. In 1977 we were ready; so it took us 4 years.

I And that organisation was for the whole of the Netherlands?

G Yes.

I And am I right that the health insurance firms, or their council, were also much involved with this? Or was that rather later on?

G Yes, no, it was parallel. The way I worked in the Health Council was that I asked friends or

colleagues in the different centres in the Netherlands to help me make reports. I didn't know anything about chromosomes, so they wrote about chromosomes. I could write about biochemistry. Still other people had to work on genetic counselling, like Ben ter Haar in Nijmegen and Martinus Niermeijer in my own department; they were more knowledgeable about this. An example of the initial attitude of our health insurers is Jan Bijlsma, who has now died. He was one of the first cytogeneticists in Amsterdam. He went to the health insurers to ask whether they could fund him for Down Syndrome diagnosis. And their answer was, I will never forget it: "Why should we fund it because I can see with my eyes when a patient has Down Syndrome; we don't need sophisticated chromosome analysis to do that." So he didn't get any funding. When I wrote my first Dutch paper on prenatal diagnosis, the insurers visited me because they saw the preventive effect. They thought, "Ah, wait a moment; here we are going to prevent suffering and a long period of high costs thanks to prenatal diagnosis and abortion." So in that way the insurance came a little earlier than our report was ready. When our report was ready, it would be impossible now, I became the only negotiator for the whole of genetics in the Netherlands. And I was sitting there two years with the insurers with my report of the Health Council. I knew them by first name; I went out for dinner with them; I got their trust; I never asked too much, but when I asked too much, I told them, "Wait a moment. This chromosome analysis costs 900 guilder, but I ask you 1,000 because we must have innovation as well." And they accepted that. And still our tariffs, our funding, is based on that system. Of course I regularly consulted my colleagues in different fields and universities.

I You're very lucky to have such forward looking policy people in the insurance system.

G Yeah.

I Yes. At this point, had any specialisation or subdivision between the different centres begun, or was that more when molecular studies began?

G The latter, because in 1979 I got an agreement with the insurers, so everything was paid: cytogenetic and biochemical diagnosis, genetic counselling and prenatal diagnosis in 7 academic clinical genetics centres. Since I had just received one or two years before a large grant for the prenatal diagnosis in my own department, I got double money because the insurance paid me as well. I went to this grant organisation in The Hague offering to give it back, but they said, "What have you done for the money?" I said, "Well, spectrophotometers and this and that." They said, "What should we do with it? We only have an office. Keep it." So for a while I was quite wealthy. Each centre had of course their own research interests; for example thalassemia and Duchenne in Leiden And there was counselling and neuromuscular disorders in Nijmegen. Oncogenetics in Groningen. In Rotterdam we had our interests and Bootsma's group had been successful in the relationship between chromosomal aberrations and leukaemia. Amsterdam and Utrecht were more problematic and Maastricht didn't exist. The health insurers wanted an organisation for clinical genetics to be independent of the academic hospitals; they wanted to be sure that money provided was really spent on clinical genetics. Very wise. This system stayed till my retirement in 2001. So I had already a chromosome section, a biochemistry section and prenatal and postnatal counselling. And the other centres copied this organisation either from existing units or they created new units. And all centres got the same tariffs. So genetics in the Netherlands as a whole became stronger. Now there are 8 centres because Amsterdam has 2 universities one based on religion and a general one. And then, of course, as you said, molecular biology came and there Leiden was the first; Peter Pearson did good work on Duchenne with Van Ommen, and there was cancer genetics in Groningen and in Nijmegen, where Ropers came later, there was also experience analysis in X-linked diseases. In Rotterdam we were not very active in the beginning, but later we started with DNA analysis in cystic fibrosis and we discovered the responsible DNA defect in Fragile X syndrome 1991. I remember I went to the health

insurance when DNA became a diagnostic tool. Peter Pearson asked my support, because I was a kind of financial father for the guys. Pearson was a good scientist but not a negotiator, so he came to me and he said. "How can I get money for my Duchenne linkage work?" So I went with him to the insurance office and he gave a lecture, and they found it very difficult, because linkage is difficult for an insurance person [laughs]. And they said, "We cannot make a tariff for such a thing." So I said, "No, give them a lump sum; and give this to 4 centres in the Netherlands". And they wrote me back, "We will give you a lump sum for the DNA work, provided that the other 3 centres that are yet not so experienced, will agree." And that was difficult, because Amsterdam, Utrecht and Maastricht had to agree. A compromise was found by saying that these 3 centres would get funding later. And in 1988 4 centres got money for DNA diagnostics and very soon after they decided to some division of labour. And this is still going on, to a certain extent, because everybody does DNA analysis in breast cancer families.

I **But it was a very forward looking idea, I think, not to duplicate for many diseases, because it also gave possibilities for high throughput, and good research possibilities as well.**

I'm looking at my list and one thing I noticed: you've written a lot of books.

G Like you!

I **True. And I'm interested that some of them are medical and scientific, but there are quite a lot, some of them in Dutch, that are more related to social and ethical aspects. Can I ask you: how did your involvement with the social and ethical aspects… how did it develop? I know that you can't help, if one's in medical genetics, you can't help but being involved to an extent; but how did this become one of your main fields of interest?**

G It's not a main field of interest, but it is the most public appealing part of interest. The reason is simple: in '72 I was interviewed by a television station with a very long interview on the ethical aspects of prenatal diagnosis, and it turned out that this TV interview was very well received. A Dutch Bob Williamson, so to say. And I got very positive comments in the newspapers: "Finally we have a scientist who can say things in an understandable way" and so on. So I was asked again, and again, and again. I must say, at that time, in the beginning 80s, my colleagues, my scientific colleagues, except for friends, didn't like it because they thought that I was too popular for a serious scientist, and they heard too often from their wives that I was an interesting guy to listen to. So they would criticize me for that. And I should become a member of the Academy of Science, but I didn't become a member of the Academy of Science. And then Dirk became a member of the Academy of Science and I said, "Well, wait a moment now; what's happening here. Look at my publication list." And one year later, I was also appointed, and I was angry. I was really angry. I went to the president, who I knew, and said, "Why was this delay?" He said, "You want the truth?" I said, "Yes." "Because of your television; they're jealous." And that's it. A matter of tradition at that time. No doctors or scientists in the news. Now from the late 90s on this has completely changed. Walter Bodmer once told me that his collaborators got training to deal with the media. Later I got prizes from this same Academy "because of your important translation of science to the public" but this was much later. I firmly believe that my television work has facilitated the negotiations with the Government and health insurers to get Clinical Genetics funded. And then I was invited by our Queen, the first time in '75, I was invited to a meeting on the limitation on economic growth, and later to talk about genetics in healthcare and the future of general health care. The first time, I was so nervous to come in the palace of the Queen and all these top people. I worked like hell on this general view on the future of healthcare. My conclusion in 75 was that it was not genetics that was the most important thing, but the ageing of the population, and the loneliness of elderly women; with increase of health problems and little future prospectives. And that had an impact on society. Many people talked about it, also in Parliament. Then I was invited for interviews in magazines, radio and television again. And again I got requests from very good television presenters, "Can you write for us appealing

programmes?" Because TV people are not so creative in a social way. So I started to write a few programmes, like a series on "All people are unequal". And I wrote two scripts for a movie: and one movie received the Berlin Film Festival Prix Future. So that was the early 80s, I think. When I had given the first lecture in the Queen's palace, some editor came to me and said, "Why don't you write a book about this?" So I did. The same period as when I wrote my 800 pages Genetic Metabolic Diseases, which cost me 3 years. I wrote a book, a kind of funny book on the life of the Dutchman. And it sold 80,000 copies in a few weeks.

I [laughs]

G Where I was used to 3,000 copies because of Genetic Metabolic Diseases in the scientific world. yeah. And this was unbelievable. Later I wrote another one; it was called All People are Unequal, with chapters about genetic difference, education, the inequality of women and men; poor and rich people and so on. And that book became a real best seller. There were piles till the ceiling of the superstores. I didn't know what happened. And politicians started to quote me, "Our head is too small for the world" and that kind of sentences. This had nothing to do with science. But I enjoyed reading about social aspects of science and also about the demographic changes in the world, the position of women, reproduction and translate the often difficult data in thick reports in a more simple way to a general public. So I've done that, with pleasure.

I You've had a lot of contacts also, I think, with different countries in terms of developing their services and influencing their attitudes. Am I right, especially with Eastern Europe originally and some of the developing countries?

G The past 20 years I have had advisory activities in different parts of the world. The United Nations asked me, in 1983 for the first time to go to China. And that was related to the one child family policy. And because of the one child family policy, the government realised that people would be very upset when they have a child with a congenital malformation or genetic disease, and were not allowed to have a second pregnancy. So they invited me to advise them about that. And probably other people as well. We came there; I don't know why, but my wife and I found it a fantastic experience. China was quite closed at that time and there were no civil airplanes yet. We flew in military airplanes and people were all dressed in Mao costumes. At the end of the trip, we met the wife of the president of China, who was in charge of Mother and Child Health. She said to me at dinner "You seem to have quite a good sense of humour and understand our people well." And how many genetic centres you recommend for our country? And I said, "Well, in Europe there is a rule made by Passarge at that time: one per 2 million inhabitants, roughly." "In Holland we have 8 centres for 16 million people. So you should have 500 or 550." And then she looked at me and said, "Let's start with 2." [laughter] I was invited 6, 7 times later to China for the last time in 2008. And the same happened to me in Cuba. They have a very good health system and their life expectation and child mortality are impressive at very low costs. Also the genetic services are the best of Latin America. I once met Fidel Castro; he invited me in his office; we spoke about inequality, about new developments and so on. He has always been interested in genetics, especially in relation to agriculture. We have trained many people from China and from Cuba in our lab in Rotterdam. We have also trained quite a number of people from Bulgaria. And I've trained people from the United Arab Emirates. Where I also visited as a WHO consultant. And that's the 4 jobs that I've done internationally, for the United Nations and the WHO. Not more. But for our scientific work I visited about 50 countries, like you, lecturing. When I retired I had lectured between 900 and 1000 times, I think. I forget. It was too much anyway. But it has taught me a lot about cultural diversity and I have acquired interested friendships.

I I can't resist asking now about the videos and films you made of medical geneticists. How, did you always carry some cine recorder around with you, or how did it happen?

G Yes, it started with the birth of our first son. As usual: small things. And I was so excited I still remember the moment; I don't know whether you have the same? But I was really excited that my wife gave birth to that first son, and I did not have enough money to buy a camera, but I had a friend, an internist, and he had a camera. I asked him, "Can you come to film my son because this is the first time in my life…" And he said, "Well, when you pay me 10 guilder for the film which had 3 minutes length." So we paid him 10 guilder. When I became a professor, my salary went up a little and I bought a camera myself. And since that time I started not to film so much my professional friends, but mostly my family. And in the beginning period, I've travelled a lot without filming, but then later I got also interested to film my national and international travelling and contacts with colleagues, some of whom also became friends. It is different when you come to people's homes, like you are here now. That's a different thing than that we meet each other in a big congress and say, "Hello, how are you?" and then we go on. So more and more I filmed countries and colleagues. First European countries and USA, then Japan and of course our visits to China. Then gradually I filmed big conferences with great geneticists like Jim Neel, Victor McKusick, Jim Watson and many others. Now Jim Neel is no longer with us; nor is Victor McKusick or John Edwards and John Evans. All these valuable people for genetics. And I'm so happy that I have their images. Maybe they're not all high quality; later the quality is better than the beginning, of course, because in the beginning I didn't even keep the original copies. So I copied copies, which made the quality bad. Nowadays I can afford to keep all the original digital videos.

I But it's a wonderful resource this, and something which I think people would value very much having made available in some way.

G Oh yes, sure.

I And that's something we should, we'll definitely talk about more.

G Yes, no, I will be happy to contribute. Your proposal of an oral interview made me think of preparing a DVD with images of all people I have filmed in Genetics and closely related fields like ethics. As you may know I have spent 7 years in the International Bioethics Committee of UNESCO. The now famous writer Alexander McCall Smith was the UK representative. Very nice and competent colleague. It would be a pity that when I die my wife does not know all the images of scientists, whereas she will be mainly interested in the children and how they have grown up. She doesn't know who Jim Neel is. And I thought it would be very good if I give this DVD to you, to the Royal Society or whatever, and then the only thing that I want to discuss with you, over the meal for instance, is how shall I prepare the DVD with the right referral to persons and names, because, as you said in this interview for an archive, you start to register and when you don't register, it's useless.

I That's true.

I've been asking everyone I've seen, Hans, two questions, and the first of these is: of the different pieces of work that you've done, if you had to just choose one, which would you feel is, has been your most valuable, or the one you feel most proud of? Whether it's something in the lab or something completely different.

G I would think, first of all, proud… I've been honoured very often, but I'm not proud. But I am probably most thankful for, in retrospect, for what we have done, what has had most impact is the training of foreign people, because there is… well, that's an exaggeration, but let's say there's at least 40, 50 countries where my wife and I can come as a tourist, so to say, and there will always be people waiting for us at the airport. And often it is a pleasure to see how they have developed and built their own group. You must have the same.

I It's a wonderful pleasure.

G Yeah, you must have the same experience. There are few people in our world who have

trained lots of foreign colleagues, often from countries with little financial means: Victor McKusik, Arno Motulsky are two examples. So that's a very satisfying activity and the funny thing is, you and I have spent our life in searching for the mechanism of gene regulation, a new protein or the effect of genetic counselling and we speak about who was first. Young scientists from Indonesia, China, Bulgaria, Cuba are stimulated by the fact that they see a whole world in front of them still to develop, be it good chromosome patterns, be it good biochemistry and especially important the development of clinical genetics and health care. Last time when we were in China, in 2008, they organised a lunch for us with most of the people who had been in Rotterdam. From Beijing one was missing, and I said, "Where is he?" Shen Yan is his name. And they said, "Don't you know what he is?" I said, "No." "Oh, he is the boss of the whole of China to fund our research." So he is now in Shanghai; he's always on the way. It is difficult to look into the future: in our lab he was not remarkable, so to say, he was modest good and very active as all Chinese guests were. But now he is the important person there. Very nice.

I It's amazing.

G Ja, it's amazing.

I The other thing I've been asking everybody is: can you think of one person, or perhaps more than one, who have been particularly important in influencing your career and how it's progressed? Either a mentor, or teacher, or someone who's had a special influence?

G My first boss, Hungarian, histologist in Leiden, creative, a difficult person who all the time thought that I was useless. He was a very critical person, but at the same time a real teacher. He could sit with me at an interference microscope that I had borrowed from the man who got the Nobel Prize for inventing the phase contrast microscope, Zernicke which was very difficult to handle. Szirmai could spend 4, 5, 6 hours with me behind that microscope to explain every detail of the optics. So were it not for him, I am not sure I would have chosen laboratory work, because initially I wanted to become an internist. And then later the Dean and founder of the Rotterdam Medical Faculty, Prof. Andries Querido, internist / endocrinologist. He was very internationally orientated and the first clinician in Leiden who combined a very high standard of endocrinology laboratory work and his clinical work. And for me he was an example of combining these two aspects: laboratory and clinic. In this aspect I differ from Dirk Bootsma. Dirk can be happy with a focus on a cell biological mechanism like DNA repair in itself; I cannot. The first thing, when I read something new in a scientific journal, is to try and see what kind of clinical, psychological or social aspects it will have. Nevertheless I have always immensely enjoyed our basic research, being intrigued by the unknown, search for understanding and guiding the 50 PhD's who completed their thesis in our department. And probably the second most influential thing are the chances that I've got to travel so much and explain to a large public what I have experienced. And also to explain the importance of new technologies and scientific progress. But it remains a great satisfaction to discover after many years a new protein or a new type of genetic defect like the trimucleotide repeat in the Fragile X syndrome. The latter was done by Ben Oostra's group together with scientists from Atlanta and Houston. I'm on these papers in PNAS, Nature or Cell and I'm proud of it, but much fades away. Because, as you know, many results in research are replaced by other research. But the other experiences I mentioned, yeah, they seem to stay more, maybe because they are related to people.

I Yes. Hans, I'm going to draw this to a close now, but are there any special things you feel are important that we haven't touched on at all, and that you'd like to say something about?

G I think we should look for a while to a few images of geneticists you know so that you get an impression about the future DVD and then my wife and I will take you out for dinner.

I Well we'll do that, and I'll close there. Thank you very much, Hans, for sharing with me -

G Let me say one thing. Do you know what I am doing now?

I No.

G I make an exhibition in one of our national museums called Boijmans in Rotterdam, and it's called Beauty in Science, and it will be open on 12th February, and I have collected about 2 years a thousand images and small films of ten different natural sciences; from physics, chemistry to geology, marine biology, genetics, Stuart Campbell's ultrasound film on the development of a human fetus, and astronomy. And I'm so excited about this new task because I've done research, clinics, books, and television, but I've never prepared an exhibition. To communicate with people about beauty is really different from talking about scientific results.

I I think that's wonderful and it's wonderful that you should be so excited about it at this stage of your life. And I must try and visit to see it.

G Yeah, do you not interview Dirk Bootsma?

I Not yet. Let me first -

G Because if you would ask me who, in the last 3, 4 decades have influenced genetics most in the Netherlands, it would be both of us, probably. Or do you restrict yourself to clinical geneticists?

I No, but the trouble is that every person I go to see gives me -

G Five other names. [laughs]

I Five other names.

G It's true. [laughs]