Herman vanden Berghe

Personal Details	
Name	Herman vanden Berghe
Dates	Born 12/06/1933
Place of Birth	Belgium
Main work places	Leuven
Principal field of work	Cancer genetics, medical genetics
Short biography	See below

Interview	
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Biography

Herman vanden Berghe (Born 12th June 1933)

Herman vanden Berghe was born in Overboelare, Belgium and undertook undergraduate research in virology and oncology on rat mammary carcinomas and their chromosomes, at Leuven University from 1954 – 1958, where he also received his MD and PhD degrees. After training in human genetics in Paris, London and Seattle, he founded first the cytogenetics laboratory (1960) and then the Centre for Human Genetics (1966) at Leuven University. The centre has developed large programmes in cell biology and cytogenetics, as well as clinical genetics, focusing on syndromology and mental retardation, employing 420 persons by 2010.

He has been a leader in the cytogenetics of malignancy and is author or co-author of 1162 publications. He was research coordinator and Vice Rector of Leuven University (1985 – 1995) and was knighted with the title of Baron.

INTERVIEW WITH PROF HERMAN VANDEN BERGHE 1st, JUNE, 2007

PSH. It's Friday 1 June 2007 and I'm talking to Professor Herman Vanden Berghe in Leuven, Belgium. Herman may I start right at the beginning and where were you born and in what year?

HB. I was born in a small town in Southern Belgium near the French speaking region and the name of the town is Geraardsbergen and that was on June 12, 1933 on a Sunday, in the afternoon as my mother told me.

PSH. And this is not so far from the southern border, or is it near the border with Wallonia?

HB. It is on the border with Wallonia and it's not far from France. It's about 35 kilometres away from France.

PSH. May I ask, your family, did they have a medical or scientific background at all?

HB. None whatsoever. My father was the first of his kindred of 8 who was able to study, because he was number six in the row and because his brothers had started working at the age of 12. And he was allowed because the local priest told my grandparents, 'this young man, you have to send him to school and not to work immediately. '

PSH. It interests me that there seem to have been several people where it has been the priest who has been the person who has identified promising young people.

HB. This is absolutely true here, because you had these what do you call them, these boys who serve in the service?

PSH. Yes, altar boys.

HB. Yes, my father was an altar boy and the priest obviously identified him as a smart young fellow, which he was.

PSH. And on your mother's side.

HB. No. A history of farming for five hundred years.

PSH. So when you started your university training was there anything that particularly made you keen to go into science or medicine?

HB. No. In my last year of high school when you had to make a choice, I had decided I would not become a lawyer, not become a language man, not go into history, not in engineering, and medicine was the only thing left.

PSH. Remind me where you did your medical training then?

HB. Here.

PSH. Here in Leuven. At that time was there a large scientific component in the medical course or was it very clinical?

HB. It was clinical with the exception of one group of laboratories. All the rest was clinical, high standards, but purely clinical. There was one exception and that building was not even at the University Hospital. It was far away, almost out of town, had been founded by a Dutchman Noyons at the end of the nineteenth century, was dedicated to physiology and was actually the place where the later Nobel prize Deduve, did his work in biochemistry, and with the exception of those four or five small labs with three or four people each, there was no organised research at the medical school or university faculty.

PSH. So when you had completed your training, am I right that you developed a strong interest in oncology?

HB. Yes. Also that was not that much of a deliberate choice. That's how it came to me you see, because I had been working as a research associate during my studies and I was preparing a thesis at the end of my medical studies on transplantable mammary tumours in rats, which I had induced myself by acetyl amino fluorene. They were transplantable so they were a nice model to test a lot of things and I followed the passage after passage morphology, the sensitivity to viruses because I had had a full training in virology as a student. And I experienced that, and this I repeated many times, at the sixteenth passage in vivo, the tumour would change radically. It was no longer recognisable as an adeno-carcinoma. It had become a sarcomatoid type of tumour had lost its hormone dependency and the virus sensitivity had changed. It was no longer sensitive to vaccinia but only to herpes. So I had the idea well, cure my tumours by injecting the rats with herpes viruses and the tumour disappeared completely but the rat too. I had some sort of natural inclination to go into oncology.

PSH. And this research you were mentioning then, did you have one year, two years full time during your medical training?

HB. No.

PSH. Or was it all just in spare time?

HB. Yes. Well even . . .

PSH. More than spare time?

HB. More than spare time. Because I spent months and months during my studies at the Netherlands Cancer Institute in Amsterdam. Also this came from a clear sky. In the lab in virology when I was working as a student we needed rats. R-rats These rats were not available here any more at the time.

So I had to drive to Amsterdam to get rats and Műhlbock the Chief of the cancer institute asked me "what are you doing here?" And I was 21 years old. I said I am working in a lab in Leuven and I'm here to get some rats and he wanted to know more about it and he said you can come here, if you want. So I went there and learnt a lot of techniques – hypophysectomy in mice, keeping the mice alive - putting several hypophyses under the capsula of the spleen of a healthy mouse thus inducing mouse mammary carcinoma in these mice, because prolactin was the only product left of the hypophyses after this transplantation. This was a model system in hormone carcinogenesis.

PSH. And all this was before you qualified as a doctor?

HB. Oh yes, years before.

PSH. Did you then complete a training in clinical oncology? Was there a formal training in that then?

HB. Not formal. It was simply being responsible for about 45 patients with different malignancies under the supervision of an internist. Doing clinic during the day and the lab during the night.

PSH. OK. Yes. At what point did chromosomes and genetics enter the picture?

HB. Again I have to go back to my rats. At the time of transformation, at passage sixteen, when they had lost their sensitivity to vaccinia, I looked at these tumours with the Caspersson UV absorption technique, and noticed that the size of the nuclei and DNA content had increased considerably. And then came the idea of looking at chromosomes, not because I believed in chromosomes. I had never seen any one and the mongolism paper had not come out yet. This was in '56/'57. So I then thought, well I would like to see what is going on in that nucleus and I went to see our Botanists, because there was nobody else available around to teach me whatever technique and they squashed like all cytogeneticists of those days. They all had a flat thumb.

PSH. Yes.

HB. I should have brought my squashing machine, because I developed a small metal block, very heavy with a long handle but with a very short, vertical momentum. And I made very nice squash preparations of my tumours and I saw chromosomes but there was absolutely nothing I could make out of it because to begin with all were acrocentric, there were bigger and smaller ones but that was all, and then they were all intertwined. I could not see any consistent patterns. That was it.

PSH. This was still rats.

HB. This was rats and this was long before Lejeune's paper came out and when Lejeune's paper came out then I said Wow! And I tried to do human chromosomes on fibroblasts starting from a plasma clot. You know the technique of those days? And I was not very successful on these fibroblasts, and I had too much clinical work at that time, it's not before 1960 when Peter Nowell published his technique on lymphocytes that I started again. So I started again in 1960 and got nice chromosomes, and within weeks the endocrinologists would be knocking at the door; we have cases of hypogonadism and would I be interested to look at sex chromosomes? Pat Jacobs' paper had come out on Turners and Pat and, Hamerton?

PSH. Yes Hamerton and Paul Polani.

HB. Paul Polani yes. So I started occasionally at the beginning, but more and more frequently after a few months, mostly sex chromosome abnormalities in endocrinology patients and of course also from the paediatricians I got samples of 21 trisomy.

PSH. Did you by this stage have a lab of your own?

HB. Yes

PSH. And was this in the pathology department here?

HB. No, it was actually in anatomy, because when I worked in the virology lab, I did all my virology work there, but I could not bring in animals there. So for the animals, I got a room in anatomy. Now the professor of anatomy and of oncology was the same man, so I got a few square meters in the basement of the Institute of Anatomy. So from rat on my desk, I got humans on my desk.

PSH. So now we must be at about 1960 or thereabout?

HB. '60 or '61 yes. I got interested in Turner's syndrome and with the collaboration of Jan Bijlsma, we set up a sort of survey of Turner's syndrome both in Leuven and in Amsterdam and made it a multi disciplinary study. I was lucky enough to identify in 1961, but I brought it to the Congress of the Hague only in 1962, a translocation between the short arm of chromosome 2 and the short arm of the Y chromosome in a patient with severe hypogonadism. So my hypothesis at the Hague was; there are one or more genes on the short arm of the Y which has something to do with male differentiation. And Lionel Penrose was in the audience and he got wild about it. Also because of my second presentation which was on mosaicism, 21 trisomy mosaicism in a mother of a mongol who was phenotypically perfectly normal, but Penrose wanted me to take footprints and fingerprints from this young lady. I visited her; took these prints, sent them to Penrose, and he sent back a letter. "I am very excited because the plantar pattern of this mother is that of a mongol and also she has some small details in her fingerprints: an open loop towards the thumb on the 4th finger.

HB. Penrose wanted me to join him at the Galton so he arranged for a WHO fellowship for me and I went to the Galton

PSH. Now I see that you went to Penrose, to Lejeune and then later on to Motulsky.

HB. Yes.

PSH. Which came first, Lejeune or Penrose?

HB. Lejeune, but I stayed there only five days.

PSH. Ah.

HB. Lejeune told me 'you have to learn tissue culture first'. You know he was working with these old recycled milk bottles, much to his credit huh? But I had been used to plastic for 3 or 4 years already. So I said to the technician, tissue culture I really do know that, on various tissues and she said yes but Mr Lejeune wants you to start with tissue cultures in these milk bottles. On the fourth day I convinced her to tell me only how she did the hydrolytic shock. She told me, and the next day I left because that was the only thing I could learn there.

PSH. Did you get any time to gain an impression of Lejeune as a person and as a worker.

HB. Well not as a worker and not as a person because he was very much involved in the clinics still at that time with Turpin.

PSH. This was still at Hôpital Trousseau.

HB. Hôpital Trousseau. And I never got to see him because he came in the lab at night and maybe a couple of times during the day but I did not get to see him. I saw him when I came in and he said to me, and he did not spend much energy doing it, he said "you have to learn tissue culture first".

HB. I said yes. What do you say because he was a very authoritative man and tres Français eh? He really held it against me that I left after five days. It was not before 1969 that we shook hands again at the meeting in San Francisco.

PSH. Did you get a chance to meet Turpin at all?

HB. Once.

PSH. And was Marthe Gautier still there?

HB. She was there yes.

PSH. And what did you feel about her and her work? I should say that I have had the chance to interview her. She's still very alive and active.

HB. Glad to hear that. But she was a very quiet person. She was working in her corner and I didn't get to talk to her.

PSH. So after visiting Lejeune rather briefly then was it the same year that you went to the Galton to meet Penrose?

HB. No no no no, Lejeune was in '60 I think.

PSH. Either '60 or '61.

HB. It was '60, and Penrose was not before the fall of 1962 after the Hague congress.

PSH. By that time had you decided to make a career in genetics as opposed to oncology?

HB. No.

PSH. Can I ask when did it happen that you saw genetics as a possibility for a career rather than just an interest?

HB. Well there were two reasons why I did not think about genetics as a career. First of all there was absolutely nothing here in genetics. No laboratory to step in with a chief. Nothing. There was no reason for genetics to be set up because there was no teaching at the faculty and there were no hospital beds. Now those are the two existential reasons for somebody to get off the ground. That's one thing. Second, I needed some sort of job security, which I did not have and it's not until in 1963 when I was appointed Associate Professor for teaching practical courses of histology to the students, a position which the Professor of Virology, in the meantime also Pro-rector at the University, had given to me to enable me to develop my laboratory. That's when it started, '63, but my vision still was very narrow at that time.

PSH. Can I ask about your time in the Galton? You had three or four months there?

HB. Yes, in total a little more, spread over two years.

PSH. I have talked with a large number of people who have spent time at the Galton. Was that time an important influence for you?

HB. I would say it was like a vision upon a different world. It opened my eyes, absolutely.

PSH. What do you think were the most valuable attributes of the Galton and Penrose?

HB. Well first of all Penrose knew genetics really well. He was trained probably in formal genetics, right?

PSH. Yes.

HB. Especially? And chromosomes, he never touched upon anything in chromosomes but he knew what it meant. I think, didn't he have a paper early in the fifties where he says mongolism must be a chromosomal disorder?

PSH. Yes he did and then tried with Ursula Mittwoch.

HB. Ursula, yes.

PSH. I am interested though that all the people I have spoken with who have spent time with Penrose at the Galton, they all have said it was a formative influence in their career, and yet, they all say it was not very well organised.

HB. No. Oh no. Except for when I got there the first day, he asked me where do you stay? I said well for the moment I am looking along Tottenham Court Road to see if I can find a small room here and then he said "no, no." I said why not? And he said "you stay with me. I have a large home with 14 bedrooms. There is only one condition. You have to play chess with me every night. "I stayed with him and played chess and he was the father of the famous chess champion. I have forgotten his first name.

PSH. I think it was Jonathan Penrose.

HB. Yes probably. I met his brother who became an honorary doctor here last year. But we would be sitting there over this chess board and he would be talking genetics, teaching genetics to me and we would have one game and then after an hour or two hours he would say "By the way I am taking your queen."

PSH. Were you quite good at chess yourself?

HB. No, not totally ignorant but not so good.

PSH. Which of the other people at the Galton then do you remember most clearly?

HB. Well she is still there. Joy Delhanty There was Mrs Holt on dermatoglyphics.

PSH. Yes, Sarah Holt yes.

HB. She taught me dermatoglyphics. At that time we would go to the other side of the road for lunch and I remember meeting with Dent, and Penrose would ask him by his first name, what is the inborn error of metabolism of the

week? That was the rhythm with which these things were being published at that time. And that's when I decided later I would never go into inborn errors of metabolism.

PSH. Yes, because it was developing just too fast.

HB. And I was struck, and we can come back to that later, by mental retardation, which was a black bottle of ink you know. Absolutely nothing was known about it and I decided, mental retardation will be one of the major research, clinical and research lines in our lab later.

PSH. So when was it you got the chance to really start to develop human genetics here in Leuven?

HB. Well the very modest start of 1963 when I got a tenured position in histology. And I had a small lab with very basic technology of those days. Lymphocyte cultures and the occasional fibroblast culture mainly on patients with hypogonadism and mongolism and a few more because in '63 I did a big survey of psychiatric institutes which included then mental retardation patients. So that's when I started to get a vision, having in my head what Penrose had told me, that this discipline will have a great future.

PSH. To begin with, was it just yourself or did you have some technical help?

HB. I got my first support from the National Foundation here in 1963 and I was able to hire one technician with that. It was 250,000 Francs. So I had one technician and then her salary would be 190,000 Francs and I got another 50,000 Francs then for materials, a working budget. That was it. I was alone. I had one technician.

PSH. And at what point did you have any other colleagues, either medical or scientific, to join you.

HB. From the beginning a doctoral student in anatomy made a tremendous contribution: Herman Verresen. When I set up this study in the psychiatric institutes I had made a call in my teaching of histology lessons: Would there be any students willing to collaborate in their spare time during the summer.And then a few of them showed up, Cassiman, Fryns, David. You see the story?

PSH. Yes.

HB. In '66 I sent Cassiman to Stanford. In '68 Guido David was to follow him, and later on Peter Marynen would also go to Stanford.

PSH. Which part of Stanford? Was it any particular lab or unit?

HB. It was Howard Cann's lab.

PSH. The same Howard Cann who then was back in Paris?

HB. Still is there and worked with Jean Dausset. Rue du Cherche Midi, that's where he lived in Paris. Yes the same Howard and Howard knew what I was expecting from him and I had said to Jean Jacques when I left him here before the town hall in '66: Jean Jacques, we don't have any money, any scope to do huge population genetic studies. But with a good tissue culture and a good idea, you can do a lot of things. So go and don't come back before you are an accomplished somatic cell geneticist. So that's what I said. That's what he did, and he worked with Merton Bernfield, who died unfortunately two years ago, on cell-cell interaction and that's what he continued here, later on. Signalling from cell to cell. Guido David also worked with Merton Bernfield and Guido would later on discover these glypicans, syndicans you know, all molecules at the cell surface wWork already started here by Fred Van Leuven. Peter Marynen wanted to come to the lab and work for one year instead of going into the military. You could do that work for one year. And he was so good I said we must keep this man so I got a fellowship from the National Foundation and sent him to Stanford also, but this time for molecular biology, because I didn't know any molecular biology. The best I had ever done was a Southern blot. But Peter came back as a full well-trained microbiologist. So I sent out people, invested a lot in the last half of the sixties and by 1972 the first came back. That was Cassiman, soon followed by David because Cassiman stayed six years. David stayed 4 years, Peter Marynen 2 years then later on it was not necessary anymore, although I have sent younger people later on to Ann Arbor Michigan, to NIH and other places in the USA. But that was the second generation anyway. So I send out and I kept the coffee warm. Basically that's what I did.

PSH. And when was it that you had more than a single lab that could act as the basis for a proper institute. When did that come first?

HB. Well in the Institute of Anatomy, we grew so much that we more or less occupied first half of the building and then three fourths of the building and the Professor of Anatomy was lenient enough to let me do it. Also there was a laboratory for electron microscopy which he gave it to me.

PSH. That was very fortunate.

HB. Very fortunate and it was run by Bernadette Vanderschueren, who has just retired now. She has done all the electron microscopic work for us. But I inherited here from her father, from the Professor of Anatomy. So it's in the late, well between '66 and '70 the idea grew and the space grew but the people, the staff were still not there. I got more technicians but it was not before '72 when Cassiman came back, also the year after that I was preparing the foundation of the genetic centres in Belgium. That was a political play not a scientific play which in '74 ended up by creating one genetic centre in every university in agreement with the Minister, and the Minister had said there will be money and there was money, not enough anyway, but I told him there should be only one canal through which the money comes through that

particular university. In other words if there were fifteen candidate laboratories, fourteen would not be funded. They would have to come to an agreement to make one centre in each university with the money made available. That worked: there are 8 centres in Belgium.

PSH. May I ask, am I right that this was rather closely paralleled to what was also happening in Netherlands and Germany around that time? I am wondering where the concept of a genetic centre in each university, was this something you thought of specifically for Belgium or were you influenced by what you had seen happening in other European countries?

HB. Not so much. I was impressed by the size of the laboratories in Holland but not by their model system because there was hardly any model system in Holland. Germany I had not visited. In France there wasn't anything. Cytogenetics was in histology for a long time. But here, it was one of my basic concepts that research and clinics should be on the same floor and that we should have a strong cell biology base. This concept was mine.

PSH. Right, yes. Was that perhaps because all the people who were working with you were all medically and clinically trained?

HB. Well I wanted them to have a double training. So all of the pivotal people are paediatricians or internists. That was what I put down for myself, the concept of the genetic clinic as I saw it in those days.

PSH. Yes. Say when you would like a break Herman.

[Break for coffee and to look at document provided by HB]

PSH. Yes this is very valuable actually to see what you have written. These points here, were they in the document that you prepared for the Ministry at the time?

HB. Yes.

PSH. I'm interested that the Ministry must have itself been interested for something to happen.

HB. Peter, they didn't know anything. Let me tell you how sometimes history works. I
was called to the Rector's house (who was the virologist with whom I trained), one evening, because the Minister of Health and the Chief of his cabinet would be there to discuss abortion. The Minister was a Catholic so he came to discuss that subject with the Rector, the highest authority of the intellectual Catholic elite. The Rector had called me in because he said maybe if you present them a few case examples of where you know that the foetus will be abnormal and that you must leave the choice to the woman, what is going to happen. Maybe the Minister will be convinced that abortion in some

cases can be accepted. And that was my introduction in genetics to the Minister of Health who told me, that seems to be interesting. What are you doing there? Come and talk to me and I came with a fully made concept of a genetics centre.

PSH. That's very interesting.

HB. But you see how things work?

PSH. I do and I'm interested. it is very different from America where there is no co-ordinated development of medical services, but here, as in Britain, it has been carefully planned but led by professionals, and government officials have responded to that.

NB. Indeed the Minister was a man who would listen and I had the big support of the biggest health insurance company here in this country: the Christian Health Insurance company supported me. I told them, look this is a new type of medicine. I don't want for this country, genetics to be a medicine by the act, payable by the act. It should be a global thing with support from the government and access for the patients should be free. We should explain to them why they don't pay. And they helped me because if Insurance companies say to the minister it will be like that, that's how it will be.

PSH. I am very ignorant, so in Belgium, is most of the health system funded through these big insurance companies?

HB. All of it. Virtually all of it.

PSH. Then that is important. Can I go back a moment, Herman, to the beginnings of cytogenetics across different European countries and ask a little about your links with other people who were developing things. Who were the main contacts you had and collaborators in other centres in the early mid sixties?

HB. With Amsterdam in the early sixties and I had some contacts with the Parisian people.

PSH. Which ones in particular, because there are number of different ones?

HB. Well there was Lejeune and his opponent De Grouchy. I had better contacts with De Grouchy than with Lejeune. Maybe because they were not too close. But my contacts with De Grouchy were not too close either. I saw Berger in those days. He was young. I saw Dutrillaux who was also, very young, but Lejeune was the leading person in cytogenetics.

PSH. How about Marco Fraccaro.

HB. I met him only late. In the late sixties at some meeting or another. He was a charming man but a co-worker of mine later on, Paola Dalcin made her

doctoral thesis with him and she told me a little about him. I think except for Trisomy 18, what was it he was involved in? He was invited to one meeting after another but did not bring new data any more.

PSH. I think most of his original data were when he was working in Sweden at the beginning.

HB. I cannot judge that, but it could be. Could very well be.

PSH. How about the Scandinavian groups? Had you contacts then with people like Levan?

HB. Not before I started working in cancer genetics and I met with Felix Mittelman (in 1977) and through Mittelman I had the privilege to meet with Albert Levan several times because he was interested in Felix's work. This was a very quiet, almost introvert, who didn't speak too much, but what he said was valuable, very valuable. I did not meet Levan as a master of thinking or for the work that I did.

PSH. Were there other people in Europe who you had close scientific links with up to that period.

HB. Bijlsma was my only contact in the Netherlands in the sixties, and I had occasional contact with Hustinx, who died 25 years ago now. There was Anders in Groningen. He was a Swiss man. He was also very introvert. He didn't say too much.

PSH. How about the British units. Did you have contact with Paul Polani?

HB. Not with Polani but with Ferguson-Smith.

PSH. Oh yes.

HB. And I spent two months in Edinburgh with Court Brown in those days. I also got acquainted with Rutovitz with whom later on I would set up the first concerted European Action on chromosome automation.

PSH. Yes I was reading that you chaired that group on automation.

PSH. And Pat Jacobs, was she in Edinburgh at that time?

HB. She was in America in those days.

PSH. She was in America.

HB. I met her for the first time in Hawaii with Newton Morton.

PSH. Yes indeed. Coming on to

HB. I met John Edwards of course . . . How is he?

PSH. John? I saw him not so long ago. He has had some problems with his walking and mobility. He had an accident, so I would say he is rather restricted by that. But yes I saw him probably only just one month ago. He is still very, well he is a very active thinker.

HB. I liked him very much.

PSH. Can I ask now a little bit later about your work on cancer related genetics, because am I right, this has always remained your own personal area of work, even as the Institute developed more widely?

HB. Oh yes, because you know I was not a very authoritative leader in my Centre. I let everybody work. Discussed the work every week with everybody but the respect that I would get, I thought, had to come from my work and not from an institution. So I started this cancer cytogenetics work in the lab and pretty soon after the 5q minus story the fellows started coming. I had dozens of fellows. I had thirty Italian ladies in my lab but they came in waves. First came the British. Denise White who worked with you in Cardiff. She is still there, Denise White with Alan Jacobs.

PSH. Yes.

HB. I was on her thesis committee with Alan. I had a lot of contact with Alan Jacobs. First came the British, then came the French. Madame Fraisse, Marie Francoise Berthéas who has just died from astrocytoma. Many French who came to train in my lab for this particular type of cytogenetics. Then came the Italians and they started coming and they continued coming. The best ones are now in charge of haematological genetics labs e.g. Antonio Cuneo and Christina Mecucci in Italy. All these are people who have come through Leuven. Whereas in the meantime Cassiman also had organised summer courses in human genetics. So there were lots of people that trained in Leuven here and most brought their own money

PSH. That's useful.

HB. Very useful. That's how the Americans survive.

PSH. What about clinical genetics. At what point did the institute begin having clinical research and service interests rather than pure laboratory work.

HB. In the sixties with the mental retardation plus syndromology.

PSH, Was it Jean Pierre Fryns who has been the main person from the beginning?

HB. No he was young. He had to train as a paediatrician first, but every day he walked in and I tried to put him in the lab which did not work but he had a remarkable clinical eye and I said one day we will need clinical geneticists

having a genetic clinic and it is not before 1974 I think that Jean Pierre comes into the picture and he took over from me. Before that time, I did all the consultations.

PSH. So you had a genetic counselling clinic?

HB. Yes. From 1966 on. Actually already before, but formally we became a division at the University Hospital in 1966.

PSH. One thing I haven't asked about so far is your time in Seattle. Now this was quite a long time after your visits to Penrose and to Paris.

HB. Yes 8 or 9 years and I got an NIH post doc fellowship to go there. If there was the Penrose window, this became the Motulsky window.

PSH. What were your impressions of Motulsky's unit and Motulsky himself?

HB. Arno's unit by 1968/69 had developed quite a bit. The chromosome unit was run by Phil Fialkow. We became close friends and the clinic was only once a week and that was about 20 percent of what I was doing here. So I was assigned to one family for that one afternoon and by the end of the afternoon, every fellow who had seen a family had to report before the audience with 25 people. Everyone was there, even the haemoglobin people. Motulsky would ask a few questions and then the diagnosis and the prognosis and what to tell the people would be discussed and every family would walk in one after another and Motulsky would tell them what the result of the discussions had been. That's how it worked, once a week. In cytogenetics I did all the bone marrows of Don Thomas' dogs which he used for his pioneering bone marrow transplantation work.

PSH. That's quite similar to my own experience with Victor McKusick and Moore clinic. I'm not always certain whether it's the best way for the families.

HB. I don't think so, psychologically not. But in America . . . Here it would not work. People would be frightened, scared to death, and they would not hear 50 per cent of what they are told. In America it is more formal. People are more used to these things. And also, a family in America is different from a family here. Here there would be ancestors up to the15-1600s and they know everybody. In America, the pedigrees that I took would be a catastrophe with Scottish, English, Swedish and they did not know anything about their family. It was a totally different clientele if I may say so. Totally different. The diseases of course were the same. I was very impressed by the genetic work on haemoglobin and G6PD that was done in Arno's unit. Those were the days of establishing the links between malaria, abnormal Hgb and G6PD, also the different types of G6PD. Motulsky had been in the Congo to collect samples.

PSH. I had forgotten that.

HB. That's why also when I wrote to him that I had done, in 1969 a study on 6600 consecutive newborns at the Kinshasa hospital, 453 parameters of child, mother and placenta, Peter, along with about 10 genetic parameters. We did chromosomes on these people We did haemoglobins. I found four Chinese haemoglobins there. Where did they come from? From the Chinese railroad workers that made the railway between Matadi and Kinshasa. I established, it was published right away in Science, that the incidence at birth of 21 trisomy and the major sex chromosomal abnormalities was the same in Kinshasa as in New York City, whereas this population in Kinshasa had never seen radiographies, yearly check ups, had never heard about the contraceptive pill. The natural radioactivity of the soil in Kinshasa was extremely low. Yet, you know, those were the big discussions in those days. Was the pill responsible for the raise of 21 trisomy with age? Same incidence. That study was fantastic. We showed that hepatitis B did not pass through the placenta unless there was a hole in the placenta or a leak. And many other things e.g. we showed that the very high perinatal mortality was due to placental malaria.

PSH. How did you come to be involved in that study in the first place?

HB . Because in 1966 Roger Eeckels, Vice Rector of the University of Lovanium founded by Leuven in '54, who was a paediatrician, wanted me to set up a laboratory there. Actually I did not have to ask for permission to bring one technician or two technicians from here to there, there would be 5 charter flights a year, you know the transport was very easy. So I set up a laboratory there, purely diagnostic, but to make it interesting I eventually did that study which was fascinating, and second, I had one biologist trained in chromosomes of fish because the Stanley pool in Kinshasa contains teliostei, contains all the actual species, plus also their presumed evolutionary predecessors are still there. Fantastic. Fantastic.

PSH. That's a real opportunity because probably even now perhaps, they've all been disturbed.

HB. Now I don't know but that was a unique opportunity, but we had to get chromosomes from fish and that's also a story. I tried everything here to get fish chromosomes. Couldn't get one single mitosis from bone marrow, from whatever I would try. The cutaneous cultures would always be infected and too much antibiotics would kill the culture and so on and so on. Until one night I thought what could be a tissue in the fish which would have say, a wave of mitosis. I had tried the intestinal mucosa, bone marrow, and all of a sudden I thought about cornea. Maybe there is a wave of mitosis in the cornea when the sun gets up.

PSH. Good heavens.

HB. It happened. At first I missed the hour because I didn't start early enough. One hour later it's gone. It's a very short wave. With beautiful mitosis which I squashed with my machine and I got beautiful chromosomes. Now that was easy in the Congo, the Lovanium university had a boat. We

could go early in the morning before the sun gets up. Get our fish. Squash them on the boat and bring the preparations back to the lab. The only problem was to get the fish. So I asked a local fisherman. It cost me dozens and dozens of crates of beer before I could convince them to deliver their secret. Do you know what it was?

PSH. No.

HB. You throw pesticides in the water.

PSH. Oh Dear.

HB. And they are popping up like in the lake of Galilee. So he got more fish than you could imagine, than you could possibly handle that day. Take e.g. these lungfish. There are 5 species. There are 4 polypteres and one protoptere. The four have the same chromosomes but the protopteres which is a family, very much related, one difference, one Robertsonian translocation, published Experientia (Basel). All this was in the late sixties

PSH. That's really fascinating.

HB. Anyway the man who was supposed to continue this work, a biologist, at one time got the panic of his life because soldiers had come into his house and the next day he fled and went back to Belgium.

PSH. Oh dear. Coming back to Belgium again, I see you've been involved with a huge number of committees, important bodies. There's only one I want to ask about because I am intrigued. You were on the Nobel . . .

HB. Nominating committee. I still am.

PSH. I don't quite know how it is organised. Does each country have an Nobel nominating committee?

HB. I do not know; possibly academies, but there are several, I think there are several people here in Belgium, in England, in France and elsewhere who are chosen by the committee. I think that the man who is responsible for me being a member of that nominating committee is Jan Lindsten, because I knew Jan very well in the 70s.

PSH. Because Jan was I think on the actual committee that helped to choose, so this is different from a nominating committee I suppose.

HB. I don't know. That's what it is called on their stationery.

PSH. But you weren't one of the ones who decided who should get it or not.

HB. Oh no no no, nominate I mean, proposed?

PSH. Yes.

HB. Propose, sorry

PSH. I think nominating is the correct word actually.

HB. Can we make a break for a cigarette.

PSH. Of course make a break. Then I don't propose to be very much longer. Maybe after the break another 20 minutes.

[Break in interview]

PSH. I was going to ask now, in terms of the other centres in Belgium, Leuven was the first genetics centre. Which came next?

HB. Formally for clinical genetics no centre dates back earlier than 1974 because actually on behalf of the minister I went around the country and founded these centres Brought people together. In Liège for example there were 3 candidates. We gathered in a café and I told them there would be one lab which would be funded. Now you can go out and shoot each other and I will see who comes back or you can agree. And they agreed to work together.

PSH. So who were they in Liège at the beginning?

HB. Frederick, and he was inheriting a family tradition of scientists. Now here in Leuven, if I can make a parenthesis, nothing was remembered of the glorious past of this university in cytology in the first half and the second half of the nineteenth century. Theodore Schell was here who worked on animal cells. One of his pupils was Van Beneden who discovered meiosis. Here, I can show you the building.

PSH. Yes.

HB. Janssens was here, who was a pupil of Van Beneden, who discovered crossovers but did not know what they meant until Morgan showed what they meant. But you know, three monuments, plus Carnoy, whose fixative is still used today.

PSH. I have to say I didn't realise those were from Leuven. I really didn't.

HB. Schwann, Van Beneden and Janssens. It's only in agronomy that there was some tradition continued and one of the labs in agronomy is called the Janssens laboratory. I wonder Peter, if at sometime the University 'top' discouraged the continuation of this type of science in medicine because it was considered to be too dangerous. You know they had heard I'm sure, about the eugenic movement. They had seen what the Nazis had done, but

they also knew what was happening already before the first world war. So I am wondering, it should be off the record but it is quite possible.

PSH. It's quite possible.

HB. So I had nobody to look at when I started and eventually in my life Peter, I never had any mentor except Penrose for a few months and Motulsky for a year but I had no mentors, no examples. I had nobody to look up at.

PSH. This is one of the questions I have been asking everybody, which is, who had been the people who had been the greatest influence in your career?

HB. I would say however short it was, Penrose, his way of thinking, his vision and Motulsky and his group, Phil Fialkow and other people who confirmed to me: Herman, what you have done already in Leuven is the right track to follow. So I was you know, confirmed in my ideas about what genetics should be. And Elo Giblett in Seattle a little bit because I worked in her lab. Did enzyme studies, phenotypes on 300 paratroopers of Mobutu, healthy paratroopers with a lot of new phenotypes that came out.

PSH. Coming back to the Belgian centres, what about Ghent.

HB. I went to see Hooft who was head of Paediatrics and I told him, Professor, I come here with a mission from the Minister of Health. We are to put up centres in every university but he didn't want to talk to me. He didn't even open the door totally. He said to me, genetics, he said it in French, connais pas, c'est de la pédiatrie, so for him like for many paediatricians in those days, genetics was paediatrics. So he didn't want to hear about it. And I went to François, you know he invited me with open arms. His pupil Mrs Maton-Van Leuven later took over. She left some time ago.

PSH. But François was in ophthalmology?

HB. Yes, but he had written a handbook.

PSH. Yes I have the copy.

HB. OK, and he didn't know anything about chromosomes or about clinical genetics in general, but he knew something about genetics and ophthalmology.

PSH. And was Jules Leroy . . .

HB. No he was not around. He was still in Wisconsin with Jim O'Brien, working on metabolic studies, 'I' cell disease. And Jules came back in I think 1964/65 to Antwerp. Became a Professor of Human Genetics in Antwerp. So the only chair there was, certainly in the Flemish part of Belgium in Genetics, the only chair was Jules, because I never got any teaching here at the University. No formal teaching.

PSH. So . . .

HB. Jules after a few year went to Ghent to become head of Paediatrics, I forgot when but certainly not before the late seventies.

PSH. Were there any other people at that time?

HB. Yes. In Brussels when I made that tour there were nine laboratories which would be candidates for a centre. It was like a snake nest. So eventually I appointed the only man who would be acceptable to all of them, because he was absolutely innocuous, was an anthropologist by the name of Twiesselman, an extremely nice man.

PSH. I haven't heard of him.

HB. No he was an anthropologist of the old school, but everybody agreed that he would be their spokesman. They would feed him of course. So Brussels was set up formally also. Eventually only one major lab emerged, that of Jacques Dumont and Gilbert Vassart in Erasmus Hospital.

PSH. Was that the predecessor to the one now run by Inge Liebaers.

HB. No that is the Flemish University in Brussels. She was not among the first centres because they didn't exist. So later on when she had established her lab and with her husband had been working on reproductive genetics, I said to the other genetic centres, listen we must give some of our money that we have to make a centre at the Free University of Brussels. And that's what happened. She was not around in the beginning.

There was also Koulischer.

PSH. Yes.

HB. Koulischer was in Brussels at first but then left for Liège and I think he was the successor to Frederick in Liège. We should also remember Anne Hagemeijer trained with Frederick in Liege and made her PhD thesis there. Then she went to Rotterdam to work with Dirk Bootsma.

PSH. Galliard?

HB. Not with Galliard, he was kind of an overall boss in Rotterdam

PSH. Bootsma

HB. Bootsma. Then she came back to Leuven. I brought her back to Leuven.

PSH. And am I right that it was Liège where Winiwarter . .

HB. I asked him, de Winiwarter . I asked him how did you get to describe 48 chromosomes? And he said 'young man', he was old you know. 'Young man' and I was very young, he said 'of all the mitoses I had at my disposal, this was the more beautiful and it had 48 chromosomes and I had counted sometimes 44, 45, 47, 48 and this was the only really beautiful metaphase that I saw and it had 48 chromosomes.

PSH. Because he really was much the closest to the true number of all the early ones.

HB. I think so. From what he told me he was.

PSH. And also reading his paper, he makes an interesting statement which was that I think he had sent samples round to different people, the same sample, and they all gave different results and he makes a statement something along the lines that although one can say it is around this number, it is quite impossible to be dogmatic because the technique is not good enough.

HB. Now I must ask you, Painter what did he do?

PSH. He was some years later and also . . .

HB. He is also mentioned. They are both mentioned together.

PSH. That's right but I think Winiwarter was at least 10 years before Painter and they both used testicular samples. I think they agreed very closely except Painter I think saw the Y chromosome and Winiwarter believed there was no Y chromosome in humans.

HB. That's it. Liège plus one in Brussels at first and a second later, Antwerp, Ghent with Jules Leroy eventually, and Leuven, plus the French University of Louvain and the University of Hainaut. Leuven was and is the first and by far the best organised.

PSH. Just to finish Herman I have been asking everybody I have seen. Is there one particular part of your work that you feel has been the most special contribution that you have made. If you had to throw away all the rest and just keep one, what would you feel is the most special to you?

HB. I think cancer cytogenetics for me, I had done in the sixties, a Philadelphia chromosome once in a while, especially for the French speaking haematologists who were still here in those days. And one day I was meeting with Sokal. I said, Gerard I am getting tired of these Philadelphia chromosomes. There is nothing interesting at that time. Why don't you send me odd things, anaemias and all these things, so he did send me from haemoglobinopathies to whatever. And then I got these refractory anaemias and out of that came 1, 2, 3, 4 cases in a row of 5q minus. Sandberg had given up chromosomes in cancer because it was too complicated and no

patterns came out. Almost everybody who was working in the field had given up because it was not rewarding. You could not get good preparations. So it looked chaotic and whatever. Now this was the very first, very clear cut anomaly that came up after Peter Nowell's and it re-opened the field. That's what I'm the most proud of yes, for my personal work. Many other specific anomalies e.g. t(11;14), t(4;11), t(6;9) and more have been described by me.

PSH. And this was all before banding techniques, or some before banding techniques?

HB. The 5q minus was before banding techniques yes. And the others. I got them, but I had to re-examine them after '71 when I went to the meeting in Paris to see an explosion of techniques you know being pinned on the wall and then I re-examined them and identified them. Also half of all the characteristic anomalies in soft tissue tumours have been described here. Half of them. I was also a founding member of the International Workshops on Chromosomes in leukaemia, I was a founding father of the CHAMP, chromosomes and morphology workshops which are still very well quoted in the literature. Also because it was my own work which I did with my hands in part. Whereas the other work I was involved I never touched anything in the lab. I discussed with the people on Saturday. Saturday would be my discussion day starting at nine and finishing at 6.30 because then I was to rehearse for the singing on Sunday.

PSH. Are there any other things you would like to bring up that I haven't asked you about before we finish?

HB. I want to stress that unlike most of the other genetic centres that I knew we from the beginning did some basic cell biology and I always thought, one day sooner or later we will have to go back to basic cell biology to see what all this means. That's why we continued cell biology and always was convinced that cell biology, basic cell biology should be a majorone of the discipline of the genetic centre.

PSH. Yes, that's very important. I'm going to finish now but there's just one very final question I've got for you. Where did your interest in the hunting horn come in?

HB. You figured that out?

PSH. It was on your CV,

HB. OK. Well I was 15 or 16 when I first heard this17th century French hunting horn which was blown by a doctor in Geraardsbergen, my home town, and I was fascinated by the sound. I had some sort of musical training. I was playing mass on Sunday, playing and singing. I had a sensitive musical ear but that sound was out of this world. So together with his two sons we made a quartet and that's how it started. He drove us to all these concourses in France, to some other hunting horn groups in Belgium.

Then I when I was a student in October and November here, I would never be in Leuven. I was in France all the time on these hunts blowing the hunting horn. Soaking up that culture because it is a very vast culture, you can't believe it. We made a film also for French and German television on the history of the hunting horn. A docu-film, wonderful. This horn goes back to the Saracens and its development happened first in Southern France and in Provence, especially, and then later at the French Court, especially Louis XIV . The Count of Champagne wrote down all these tunes which existed long before, but he wrote them down in the first years of the 18th century. Now this whole music, this tradition, was brought to Bohemia first by a count of Bohemia who had spent some time at the court of Louis XIV after a tour of Italy, they had to learn diplomacy, you know, and he sent his two major hunt surveyors to Paris to learn hunting horn and that's why in Bohemia you have such a tremendous amount of scores for the french hunting horn. Rosetti Rössler wrote 43 horn concertos, and he and his collegues like Punto brought this music to Mannheim, later on in Mannheim we have the Stamitz, also Bohemians.I In the music of the early 18th century you have hunting horns in Germany which itself had no French hunting horn tradition and that's where Mozart got into contact with that. So the last movement of the four horn concertos, of Mozart is a French hunting horn fanfare. And then of course you have Lully, Delalande and all these people in France, it's full. Even Carl Phillipp Emanuel Bach (*1714-1788) in* his clarinet concerto uses a French hunting horn fanfare. Wonderful.

PSH. That's taught me a great deal. I knew nothing about the French hunting horn before. Well Herman I am going to finish now. Again thank you very much for really a very interesting account.

End of interview.