Helge Boman

Interviewed in Bergen, Norway by Trine Prescott

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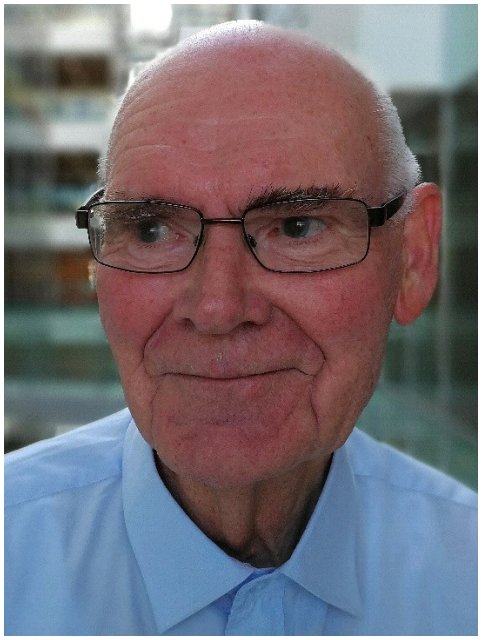

Helge Boman was born on August 26th, 1937 in Stavanger, Norway. He obtained his MD in 1962 and his PhD in 1972, both at the University of Oslo, Norway. His doctoral thesis, *Studies on Inherited Antigenic Variation of Human Serum β-lipoprotein by Passive Hemagglutination*, was based on seven articles he wrote while at the Institute of Medical genetics in Oslo (1967-72). His internship (1962-1963) at Lillehammer hospital (six months of Internal Medicine and six months of Surgery) and in a primary care practice in Vinstra (six months), was followed by a year (1964) of military service in the Norwegian Air Force (six months in Andøya, six months in Lista). He was a resident in Internal Medicine at Aker Hospital in Oslo from 1965-67. After three years (1972-75) as a postdoc at the University of Washington in Seattle, Washington he returned to Oslo. He left in 1981 to become the first professor of Medical Genetics at the University of Bergen in Norway. He was a part time consultant at Haukeland University Hospital in Bergen from 1983. He has worked on issues relating to Medical Genetics as a member of national and international committees and organizations including the Council of Europe. He was instrumental in establishing the first academic training program in genetic counseling in Norway, at the University in Bergen. His research has focused on the genetics of cardiovascular disease and rare disorders. He retired from his position as Head of the Department of Medical Genetics and Molecular Medicine at Haukeland University Hospital in Bergen at age 60 and from his position as a full professor at the University of Bergen at 70, but continues his research in a 10% consultancy position.

TP: Let's introduce ourselves. I am a clinical geneticist currently working in Skien, Norway.

HB: I began work in Medical Genetics in 1967, and have been a clinician, teacher and researcher. I retired from my hospital position in Bergen at age 60, and from my university position at age 70, but have been able to continue as a consultant part time for the hospital. My areas of interest have included the genetics of cardiovascular disease and rare disorders as well as genetic counseling.

TP: I remember clearly the first time we talked about 15 years ago, when I was a trainee in Medical Genetics in Oslo. A colleague described you then as very kind and very smart, but also as someone who didn't suffer fools gladly. I needed help with an unexpected finding, a trinucleotide repeat in the intermediate range in HTT. You did some probability calculations that were important for interpreting what the allele could mean for the individual in question and for her descendants.

HB: I don't remember that episode.

TP: Well, you have helped many a colleague, many a time, and are known for your calm analytical approach to difficult problems. But switching gears: tell me about your family's background.

HB: My father's father was a Swede born in 1844 when Norway was still part of Sweden. He was head of a paper factory. My father's mother, his second wife, was thoroughly Norwegian, from Gausdal. She was originally a helper in my grandfather's and his first wife's home. My father, Thorleif Boman (1894-1978) was a prominent pastor in the Norwegian Lutheran Church, and through his writing an active contributor to public discussions. His doctoral thesis, which compared the Greek and Hebrew ways of thinking, was published in German in 1952, and subsequently in English, Japanese and Hungarian. My mother was Swedish, but mastered Norwegian well enough to teach it in Norwegian primary school. So, I am ¾ Swedish, the youngest of four siblings.

TP: Where did you grow up?

HB: I was born in Stavanger, but lived in Drammen during the War, and until 1947, when we moved to Oslo. I started in 4th grade at Vinderen public school and went on to attend Oslo Cathedral School, a public high school.

TP: You went to medical school in…

HB: Oslo. Finished in 1962.

TP: Why medicine?

HB: In order to postpone deciding what to do. At the same time, I was getting a broad education on which I could build in many directions.

TP: After medical school?

HB: I did the 1 ½ year internship required for licensure. I spent a year at the hospital in Lillehammer, did six months of Internal Medicine and Surgery each, and then six months in Family Medicine (Vinstra). I then did my military service in

the Norwegian Air Force as a physician – six months in Andøya in northern Norway and six months in Lista in southwestern Norway.

TP: And then you married Kari.

HB: Yes.

TP: Tell me a bit more about you and Kari. And about your children.

HB: Kari and I first met at a Christmas party – she was 14 and a student in a class my sister was teaching, I was 20 and in medical school. From that time on it was only us. She worked as a physical therapist at the hospital and managed our household with two children. Unfortunately, she fell prey to some nasty microbes while we were on vacation in 2005 and died suddenly. Our son is a researcher in mathematics and data science in Albuquerque, New Mexico. Our daughter does sheep genetics in eastern Norway. Both have PhDs.

TP: Back to your work life.

HB: I was a resident in Internal Medicine from 1965-67 at Aker Hospital in Oslo. Dr. Erik Myhre, who was a friend of my elder brothers, from Drammen, organized a month long research leave for me. In early 1967 I went to the Institute of Forensic Medicine to study the Lp(a) and Gc serum system. This resulted in a paper. I also studied 20 - 30 samples from myocardial infarction patients I had brought with me from my department at Aker Hospital, and was thrilled when many of them were Lp(a) positive. I was then informed that Kåre Berg, the discoverer of Lp(a), was returning to Oslo from the US in the summer of 1967. He needed people to build an Institute of Medical Genetics and I applied for a position. Professor Berg started June 1st and I started September 1st (as his first employee) in 1967. The pay was meager, about 2/3 of my already low hospital salary.

TP: Where was the Institute of Medical Genetics in Oslo located in the early days? Who else was there?

HB: During the first years, we were in a building called “Drengestuen”, literally “the servants’ quarters”, on property owned by the University of Oslo -- an old, dilapidated building. Tobias Gedde-Dahl and Carl Birger van der Hagen were there. Anton Brøgger had just left. In 1968, Harald Torsvik who studied patients with lecithine cholesterol acyltransferase deficiency joined us. He was followed by Arvid Heiberg in 1971 and Karen Helene Ørstavik in 1972. By then we had moved to another temporary location – where a single barrack left over from the war housed the cytogenetics lab.

TP: What sort of lab resources did you have?

HB: As a young scientist, I had meager resources. We had hardly any money with which to buy things. I had to wash the disposable pipettes used by the professor’s technicians before I could use them, and then wash them afterwards so that they were ready for the technicians the next day. I used self-made columns (hydroxyl apatite) to prepare the lipoprotein samples – and placed them on the wooden stairs to the cold attic. It was winter and I chose which stairs to use according to the temperature.

TP: But you chose Medical Genetics nonetheless.

HB: Yes, genetics fascinated me. My career began in those early days and I have not regretted the choice I made then.

TP: The tools you had in the early days were taking family histories, doing Bayesian calculations, making clinical observations, studying proteins and eventually, g-banding. Anything else?

HB: That sounds about right.

TP: Tell me more *about your PhD.*

HB: Professor Berg did not allow me to do more work on Lp(a) -- he discovered it, it was his. I was given a different lipoprotein system to study – the Ag system – and the key was supposed to be passive hemagglutination. Professor Berg came up with the idea of investigating this system while in the US; his technician there tried and failed to perfect the technique. In the end, I published seven papers on antigenic variation of serum β-lipoprotein in humans using passive hemagglutination, leading to a PhD in 1972. I doubt anyone else has tried the method since.

TP: Then came your years in America.

HB: Yes. Shortly after my dissertation my wife, our two children and I left Oslo for Seattle. I had received a NIH grant to do further research in cardiovascular disease. We thought we were going for a year. I met Arno Motulsky from the University of Washington in Paris in 1971 and he was willing to accept me as a resident in Seattle. I worked on heart attacks for three years. Motulsky was amazing to work with – he had all the best qualities, personally and professionally.

I was interested in Joe Goldsteins's work; he went on to win a Nobel Prize. However, I couldn't make sense of all the data he had published. I tried clarifying the issues with him over the phone, but without success. Motulsky suggested I go to Texas to follow-up with Goldstein, which I did. Goldstein said that some "details" were too complicated for others to understand, so he had simplified the data a little. Jurg Ott worked my data.

TP: Did you do any clinical work in the US?

HB: Yes. The junior doctors did a joint session with their senior colleagues in the hospital once a week. This was how I learned genetic counseling from Motulsky and others including George Stamatoyanoupolis, Gil Omenn, Philip Fialkow and Judy Hall. Jan Friedman and Tom Bird were among younger colleagues who became well known. Many friends from that time have visited us in Bergen.

TP: And was it in the US that you started to think about establishing genetic counseling as a profession in Norway?

HB: I had the opportunity to hear a lecture by a nurse in 1974 about genetic counseling at the American Society of Human Genetics meeting in Portland, Oregon. Sarah Lawrence College already had a program. The talk I heard in 1974 led with time to establishing the first Nordic university-based program in genetic counseling, in Bergen.

TP: Who did you recruit for this?

HB: My first choice was Britt Hamre. I had all sorts of problems convincing the hospital that although she was a nurse, she shouldn't be paid as such, and that her boss should not be a hospital-based nurse. When she quit, I asked her advice about who to approach to fill her position. She suggested Cathrine Bjorvatn who was instrumental in creating the two year Masters program in genetic counseling in Bergen.

TP: Back to Seattle. Were you tempted to stay?

HB: Time went by quickly and we ended staying for three years instead of one. I was then offered a position heading up cardiovascular genetics. I wasn't sure what I wanted to do, but I wanted our children to go to school in Norway.

TP: So back to Oslo in 1976?

HB: Yes, back to my old job in Kåre Berg's department. In the late 1970's professor Dagfinn Aarskog (1928-2014) – a medical geneticist and the head of Pediatrics in Bergen -- came to visit. In 1979 I became aware that he was looking for candidates for a position in Medical Genetics in Bergen. He aimed to establish a professorship at the University of Bergen analogous to the one Oslo. The federal government approved funding in 1980. I hadn't contemplated going to Bergen before. In fact, I had never even been to the city and hadn't considered applying. However, I was "asked" by Kåre Berg to apply. His suggestion sounded like a command.

There were four well-qualified applicants and I got the job although I was ranked number two.

TP: So you moved to Bergen in…

HB: No, the first year, 1981, I commuted to Bergen by train about every second week. There was nothing to work with. No colleagues, no office, no money… in total, nothing. After a year of this, I was ready to give up and said that without an office I would resign and go back to my old job in Oslo.

I was then given professor Bergsjø's changing room in the Women's Clinic as an office. Empty, of course.

TP: How long were you a one-man department?

HB: Four years, from 1981 to 1984, until the university provided funding for a physician and a technical assistant. After another two years, the federal government gave the hospital designated funding for seven positions for prenatal testing for chromosomal disorders.

TP: Prenatal diagnosis of trisomies was an early chapter in Medical Genetics in Norway. How did it begin?

HB: We'd looked at how we could do prenatal diagnostics in Bergen for chromosomal disorders – how many positions and how much space we would need. But, there was no space for a lab at the Women's Clinic or anywhere else. Prenatal diagnosis was defined as a national task, possibly to allow each of the five university affiliated hospitals to avoid discussing whether to offer the testing. However, the federal government did not take responsibility for providing genetic counseling or laboratory testing – that was left to the hospital.

TP: When did you get a hospital appointment?

HB: Initially, the hospital director favored keeping Medical Genetics a part of university-based preclinical medicine. However, Aarskog was on the hospital board and argued the case for a joint university-hospital appointment, and I was given an adjunct position as a consultant at Haukeland University Hospital in Bergen in 1983.

TP: And how did your department start to grow?

HB: The hospital and university collaborated to build a huge building, "the central block". All space was spoken for long before the building was raised. Nevertheless, I managed to get the university to give me a small internal room with a window facing a surgical facility and a windowless storage room across the hall. Altogether, I guess it was less than 20 m^2. Empty space, of course. By this time, I had an assistant professor and a technician. They were funded federally. I still had no budget. I was told to be happy with the positions I had been allocated. The federal government had little money and the medical faculty at the university had nothing to spend.
We wanted to offer general clinical genetic services including genetic counseling, but the hospital didn't see its way clear to fund these activities.

TP: Meanwhile trying to build a department must have compromised your ability to do research.

HB: It did. My research suffered during those years. I had worked on lipoproteins for some ten years. But in Bergen the need was different. I had to say farewell to the lipoproteins and coronary heart disease.

TP: So you developed an eye for families with interesting rare disorders. Looking back now, would you rather have worked with the genetics of rare disorders or of cardiovascular disease?

HB: With both.

TP: Lars Fauske and Jaran Apold were among the people who were hired early and stayed for a long time?

HB: Correct.

Lars was originally a chemical engineer who had ended up in healthcare serendipitously, in Aarskog's chromosome lab.

Jaran Apold, my assistant professor from 1984, had no experience in Medical Genetics. I had asked for a young physician whom I could teach from scratch. Jaran Apold had been highly ranked in competition for an academic position in Pediatrics. The university felt, however, that Medical Genetics, not a very important discipline, would suit him. He started to work with Kjell Kleppe, a preclinical person who had DNA as a field of special interest. Kjell Kleppe actually described the PCR method before Kary Mullis (who was awarded the Nobel Prize for the discovery in 1993).

TP: I associate Jaran Apold's name with phenylketonuria (PKU). In Norwegian, this inborn error of metabolism is often referred to as Følling's disease because the Norwegian physician Ivar Asbjørn Følling described it in 1934.

HB: Working with the PKU registry in Oslo, Jaran obtained DNA from more than 100 PKU parent-child trios. We were able to make a molecular diagnosis in all cases except one, in which we only found a single mutated allele.

TP: You moved again in 1986-1987 and the department grew a bit more.

HB: Yes, we relocated to the Pediatric Clinic when it was being rebuilt. We were given an office, two additional rooms and a space to use as a laboratory. The national government had started to fund prenatal testing, so I was given funding for a secretary, two physicians and some technical assistance. This was something different. Now we were in the mood for starting the new service.

We moved to an old building, which had previously housed the admissions and X-ray departments. Asbestos had to be removed and remodeling was necessary. We were invited to suggest how the new facility should look. With the architect and some officials, we traveled to the Kennedy Institute in Copenhagen and to Lund in Sweden, to learn what they had done. Now, nobody was going to laugh at us!

Still, all funding for Medical Genetics was allocated nationally via billing for prenatal testing. The hospital did not provide financing for genetic counseling or any other genetic services. Thanks to the federal government official Grete Gjertsen, we were able to take the first steps in organizing a department.

TP: Say a bit more about establishing the laboratory.

HB: Haukeland University Hospital in Bergen has the oldest cytogenetic laboratory in Norway according to Dagfinn Aarskog. A young physician, Ole K. Harlem (1917-2003), who later became the editor of the Journal of the Norwegian Medical Association, worked in the Pediatric Department from 1957-1959. He managed to visualize the 47 chromosomes in Down syndrome. From that time on, with some interruptions, there has been a chromosome lab at Haukeland University Hospital. We started karyotyping cells cultured from amniotic fluid in 1990 or 1991.

Aarskog used the lab to look for chromosomal aberrations in hypospadias. He didn’t want to relinquish the lab, but it became obvious that he would give in when we hired his only technician as the head of the cytogenetic laboratory in the Medical Genetics department.

TP: Aarskog, like Følling, is a name that has become attached to a rare disorder.

HB: Aarskog was “the father” of the X-linked Aarskog syndrome. He wanted to see the mutation detected in the first family he described. Without telling us, he shipped a sample to America in an attempt to achieve a molecular diagnosis. No mutation was found. So, for his 70th birthday, we gave him a report from our lab – seven instead of eight C’s at a certain location in *FGD1*.

TP: So by 1988 you had more space and five or six bioengineers, including Gunn Pedersen who came to you in April 1987 (and has been head of the department since June 2005). DNA testing was arriving.

HB: In October 1988, in addition to me, we were seven people working on prenatal diagnosis plus two people funded by the university. The DNA laboratory was started based on PKU-testing. G272X was a Norwegian founder mutation. Genotyping was still difficult. The method we used required electrophoreses,

large X-ray films and analysis of four lanes. It was hard work to detect the coding sequence of only a few amino acids at a time. We got the sequence from the pioneer Savio Woo in the US. Computers were not common in those days.

TP: Your department was the first in Norway to acquire a DNA sequencing machine.

HB: That's right, in 1988. Using large X-ray films was immediately replaced by the new technology. We made our own primers until they could be purchased. The DNA laboratory was run by Hans Geir Eiken and much of the honor for implementing DNA testing diagnostically is his. When he moved to study the bear's DNA in the far north, his PhD student, Per Knappskog, took over in 1991 and has been here since.

TP: What have you enjoyed most work-wise?

HB: The developments during the last years have been especially satisfying. Being able to give answers to patients and their families.

I have had the great opportunity to see many patients get a molecular diagnosis. For instance, in the case of the "CISS brothers" (together with the Israeli sisters), 23 genes were sequenced before we hit the correct one (*CRLF1*, 2003). Since then, we've published around 40 papers on many different genes -- some new, some known.

I have some pedigrees from the beginning – a large pile of A3 size paper with the origins of many western Norwegian families. It was simple to make the diagnosis when we had a common stretch of DNA to search.

TP: I remember you bent over large pedigrees, haplotyping manually with colored markers.

How about teaching? You taught medical students, too.

HB: Of course. That was a primary task starting in Oslo, together with Carl Birger van der Hagen. I taught students in Tromsø and Trondheim as well. We had an 18-hour course that was continued for many years, also after I left for Bergen. I have held courses for public health nurses as well.

TP: And I heard somewhere that you taught meiosis by dancing…Other activities or involvement you would like to mention?

HB: In 1984, the Norwegian government established a committee for quality assurance of medical genetic services on which I served until it was dissolved in 1992. I was appointed to the Council of Europe's committee "Screening as a tool of preventive medicine", and served as chair. Much of the job was really done by a Dutch lawyer. Our work resulted in a recommendation by the European ministers in 1994. I also served as an observer in another committee later on.

TP: The last paper you co-authored was published in The American Journal of Human Genetics this year. You are 80 this year. Retirement, such as it is, thus far?

HB: With the hospital taking over all the genetic services, I decided to step down as department head when I was 60. Thereafter, I continued at the university, though continuing to glance sideways at what was going on in the hospital. I left

my position at the university when I was 70. I have been kindly allowed to stay on as a consultant for the hospital in a 10% position for as long as I can manage. The hospital department is currently run by Gunn Pedersen, as I said, she was one of the very first technicians I hired and has done an excellent job.

A few years ago, we finally were given lab, research and office space on the 6th floor of the new laboratory building. Consultation rooms are below on the 2nd floor. Thanks to Gunn I am still in my office, brewing coffee for *half the department*.

From the 1st of January 2018 the department will change its name from "The Center for Medical Genetics and Molecular Medicine", back to the "Department of Medical Genetics". The research unit has become an integrated in the department and as of today has about 25-30 externally financed positions *at any given time – these are people who spend most of their working day in the department*. *An additional 85 people are on the hospital's payroll.*

TP: We're getting towards the end of this interview. A hypothetical question. You're hosting a dinner party and can invite just a few people, living or not…

HB: Arno Motulsky, for the reasons I have given. Karen Helene Ørstavik because she cares about patients and their families and because she is a lovely person. Gunnar Houge who came to the department in 1996 and has meant so much for international collaborations. And of course, Gunn Pedersen. Gunn and I have had the same pioneering spirit – and we enjoyed working long hours to build towards the department as it is today.

TP: What an amazing ride you have had during your 50 years in Medical Genetics. Starting with passive hemagglutination, and then founding a new department consisting only of yourself to begin with and ending up in the very frontline of Medical Genetics. Things you regret or found particularly satisfying along the way?

HB: I would have liked to have done more. I have always enjoyed giving back to patients and their families.