Anton Brogge & CB van der Hagen

Personal Details

Names	Anton Brogge & CB van der Hagen
Dates	
Place of Birth	
Main work places	Oslo
Principal field of work	Human cytogenetics in Norway

Short biography

Interview

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INTERVIEW WITH CARL BIRGER VAN DER HAGEN AND ANTON BROGGE, 5 SEPTEMBER 2005

PH = Interviewer (Peter Harper)

AB = Antone Brogge

CH = Carl Birger van der Hagen

It's Monday 5 September 2005 and I'm talking with Carl Birger van der Hagen and Anton Brøgge about the early years of human cytogenetics in Norway.

PH At the time when people in Lund were discovering the human chromosome number, was there at that time any attempt at human cytogenetic work going on here in Norway?

AB No it wasn't; it was the paper in the Lancet on 1 April 1959, where I think it was the publication of XXY with Klinefelter and X0 with Turner, and then Jan Mohr was reading this and thought we have to do something about it. I had just finished my studies in botany, but I worked also with chromosomes of ferns, with some terrible seventy bivalents, so the chromosomes were some 140, but we studied of course meiosis. And I was asked whether I would be interested in working at his institute, which was then a very small laboratory. Actually there was only one research person there at that moment, that was Dieter –[?]-- I think because you came, [C B van der Hagen], a little bit later. There were two medical doctors. I was a biologist, but he also engaged you and Tobias Gedde-Dahl.

CH That was in '61.

AB In '61?

CH Just after summer '61. In August '61 we started.

AB So we started, and decided to try to make preparations with this short term bone marrow method. So that was what we started with and we did some preliminary work, but with no success in the beginning, but I went for two days to Albert Levan in Lund and saw how he was preparing, so we managed already then in the Autumn, starting with mostly Down's syndrome, and worked with this and of course we got also a lot of questions from people with Klinefelter patients and Turner patients and also some other types. So actually we were trying to cover the whole thing and you know, at that time there was so little published. You could just walk around and do the botany, so to speak, to look for variations.

PH So that first year or two then, was it entirely bone marrow you used?

AB Yes, then I read just a note from the American Human Genetics Society, I think, where Nowell and Hungerford, or was it Nowell I think, he presented that he had been able to study blood cultures and make preparations.

CH From the buffy coat.

AB Yes. And then of course we decided that must be much better than troubling with all this bone marrow, on small children, that was not very nice. And we started, but we thought there was a point of getting rid of the red cells. So we started with Dextran and making very nice preparations, but we didn't see any mitosis. So I wrote to Nowell and I said how do you get your mitosis? We have the cells, we have the medium, everything, and then he said, you should use phytohemagglutinin.

So when was this, must have been in the autumn of'61 I think

CH That's right.

AB just before you came, and then we established the blood cell cultures with whole blood, also because in the beginning the phytohemagglutinin was used to get rid of the red cells, but there was no point. It wasn't necessary, but they stimulated the leucocytes.

PH I'm interested about your visit to Albert Levan because it was my impression that once the chromosome number was established, Levan went back to cancer genetics entirely and wasn't really concerned in the human, clinical side of genetics.

AB So what he showed me was actually how he prepared mouse chromosomes from ascites tumours in mouse, but I mean the technique was rather similar. So we got them on bone marrows, so alright. We used something like, I think we used 8 hour cultures, established in the morning and then we did the harvesting in the evening. But then, which you didn't mention, but at the same time as you had 21 chromosomes with Down's syndrome in France, there was also the group of Jan Böök in Uppsala.

PH Correct. I should have mentioned that, with Marco Fraccaro.

AB That's right, he was the one who really . . .

PH And then Jan Lindsten.

AB Yes, as a young student

PH Yes.

AB So of course Fraccaro was the man who established the cultures. He knew how to culture. They used skin biopsies, I think that was also before I came, before you came I think?

CH Yes.

AB I went to Uppsala also to see how they made up the cultures of the skin biopsies, so they used actually both.

PH Were both Fraccaro and Lindsten, were they both in Uppsala at that time?

AB No Fraccaro wasn't there and Lindsten was a medical student, so I didn't meet him, so I only met Böök.

PH Did Böök actually have much involvement with the practical lab work? I understood he was a clinician.

AB That's right, the lady who was doing the work was called Bartha Santesson and I'm not sure whether she was a clinician or academic. I'm not sure.

CH She is on the first publications.

AB That's right, she is on the publications and she had learned the culture methods from Fraccaro, but I think he was back in Italy at that time. And Lindsten, I guess he was a medical student, I wonder even if he studied in Stockholm and not in Uppsala. I'm not sure about that. I met him later and he was actually my opponent at my dissertation but that was in '67, so that was quite later.

PH I think you are right, I think he did go back to Stockholm. I have spoken with both of them and yes, it's important not to forget that group as they made some rather early contributions.

AB Lindsten worked with various sexual deviations I think, mostly Turner's wasn't it? I think this work was done in Uppsala, Lindsten's thesis work.

PH One of the things which interests me, and I have come across since seeing both Lindsten and Fraccaro, was also the first report of triploidy from that unit, which I think was from Santesson and Böök.

AB Yes that was, and Böök with this child.

PH And there seems to have been some uncertainty about whether this was truly a mosaic, or quite what was the situation.

AB What came out, and it wasn't the first high number, was that in the tissue culture from skin.

CH I can't remember.

AB I think it was skin, but when I studied the blood it was more normal, 46 I think. So he must be some kind of mosaic then.

PH Which year was it then CB, when you started?

CH . I started out actually, not with cytogenetics, but with growth retardation. So it was in the fall of '62 I started, because then the demand for clinical investigations into chromosomes was so great actually.

AB We had a lot of things to do so, we needed more people.

PH So were you already with Jan Mohr at this time, working on growth retardation?

CH Yes.

PH I see, and you had completed your medical training before joining Jan Mohr?

CH Before joining. Actually Tobias and I, we started, he got some money from the United States, NIH money, just to do some clinical observation, and Tobias started on skin blisters, of course, and then I started on the growth retardation, but it soon turned out that there were so many types reported, so heterogeneous, so Jan Mohr wanted to establish a more clinical service, so I joined then. Of course I learnt from Anton. He had already established a lAB

PH So really were you then the first clinical geneticist attached to Jan Mohr's unit.

CH To cyto. Yes maybe you could say that.

PH So then how did things evolve from a time when there was yourself as a scientist, Anton, and you CB with a clinical background? Did this alter the pattern of development of the unit do you think? How would you see this?

CH I think so, because it led to genetic counselling with those pairs, because that was a medical service and Jan was not particularly keen on giving counselling to these parents, so I did.

AB You did the work.

CH I did the work with counselling coming from these families, and besides that Jan managed to establish to pay a fee for the chromosome analysis.

PH From the Health Service?

CH From the Health Service. So that really took off and the whole lab was financed by this payment from the health service.

PH What year was it you first started to have a genetic counselling clinic then?

CH It must have been the end of '62 and beginning'63.

AB I think so, because that started really immediately.

CH Seeing patients and going to look at patients at one or two of the institutions for the mentally retarded. And there you met the parents.

PH Would I be right in thinking that was actually probably the first genetic counselling clinic in the Scandinavian countries?

CH Well, Jan had actually in his programme, there was an opening for genetic counselling and he did some counselling, especially on Medelian disorders before the clinical cytogenetics, and so in the programme for the genetic register there's a post concerning counselling in families. So he did some counselling with some families before that.

PH Because my understanding, certainly from the Swedish centres, was that for many years they very much stayed with the basic science rather than - in Lund it seems it was not developed into anything clinical, and possibly not really so much in Uppsala.

AB Probably later. Felix Mitelman was the one who established these in Lund but I think that must have been from '69/'70 or something like that.

CH So we had a lot of counselling actually before the mid sixties.

PH What type of key developments in the evolution of things here in Oslo would you say? What were the main important points?

CH Of course it really took off when Kåre was appointed.

AB '67 yes.

CH In '67, because he came with a lot of energy and had a good reputation for doing and had won some awards, and managed to contact and to have a breakthrough in both the university and, I should think so in the medical authorities, for something really had to be done.

AB I think that Jan Mohr got the position of associate professor in something like '62 and I remember he came from a meeting in the faculty, and saying "now we have penetrated in the faculty ". They had really realised that genetics is a subject for research and you know the reason, maybe, was that our first great geneticist, Otto Lous Mohr, who was the uncle of Jan Mohr, he of course was working with Drosophila and he was a Professor of Anatomy. So Jan Mohr used to say that they all thought in the medical faculty that this genetics was something with some flies in the corner, where a Professor of Anatomy could work with it.

CH He actually continued. When I was a medical student we had a course in Drosophila by Jan.

AB That's true. Yes.

CH That was in the early fifties. Fifty four or so.

AB His position was an amanuensis position.

CH Yes. And so one mustn't forget that Otto too did a lot of publication of cases and published the clinical conditions.

AB Yes that's true, and he wrote a book on medical genetics actually, something in the thirties I think. By Otto Lous Mohr.

PH Was that ever translated into English do you think or not?

CH No.

AB No I don't think so.

PH What was his middle name by the way? Otto Mohr's middle name, because I often hear it.

AB Otto Lous Mohr.

PH OK. Because he seems to have really been a big influence quite apart from his Drosophila work.

AB Yes sure.

PH And one of the things which I can't remember, C B, whether we were talking about this or whether I was asking Jan Mohr about it, his opposition to the eugenics programme must have been rather important.

AB Oh yes. It was, yes. And actually they kept the eugenics people out of the Norwegian Genetics Society. They were never elected as members, any of them, like Mjoen and a couple of others .

PH Was this before the war or after?

CH Before the war.

AB This was in the thirties

CH Twenties and thirties. There was a lot of newspaper debate and Mohr is strongly opposed to Mjoen's. . .

PH Otto Mohr

CH Otto Mohr opposed Mjoen's ideas of eugenics

AB Together with the Professor of Zoology, Christina Bonnevie, and she was also actually working in genetics and was together with Otto Lous Mohr in creating the first Institute at the University.

PH Do you think their opposition was entirely from their own opinions, or did they have international links with other geneticists?

CH You can see that in Otto Mohr's papers, that he had a lot of contact and that was in particular because Mjoen tried to be the Norwegian representative on some international societies and Otto strongly opposed that, so he succeeded more or less in keeping Mjoen outside, so the representatives from Norway were not eugenicists but Otto and Christina Bonnevie.

PH Was there a lot of contact do you know with Lancelot Hogben at that time? Was his a name which . . .

AB Yes, he was invited as a speaker I know on the evening of the 8th April 1940 as a guest speaker and he had certain troubles in getting back to England, because in the morning the Germans arrived in Oslo and the wife of Otto Lous Mohr was going to drive out to the airport with Hogben to catch the plane to London and on their way they met the first Germans marching into the town, so she realised there would probably be no plane to London and they managed to get him out to Sweden and went all the way to

CH Over Asia

AB Over Asia to the States, back to England

CH I think he has written a book about it .

PH He has. There is a very nice autobiography, which was only published after he died actually. I think his son put together this unpublished autobiographical essay. I have it and now I remember you are quite right, it is in there that he was in Norway at the time, and then actually had to escape across Sweden.

AB Then of course Otto Lous Mohr had the connections with the fly lab, because he spent two years in New York with Morgan and collaborators.

PH What happened actually then during the war? After the Nazi invasion, was there strong pressure then to put the eugenics proponents in charge and implement things? What actually happened?

CH Yes there was actually. It is in one of the books, but not at the University level. More at the organisation of the health authority level, some of them, in charge.

AB There was a young man who was going to be, because the University was closed, but they made some changes with the Institute, so I mean Lous Mohr and Christina Bonnevie were out of the genetics institute and they appointed –[?]--who was a young man, but he wasn't particularly eugenics. I think he wasn't a eugenicist, but they didn't do much I think actually.

PH So Otto Mohr and Christina Bonnevie were actually dismissed from their posts, or just dismissed as directors?

CH I think Christina Bonnevie had died before, didn't she die in '39?

AB No '48.

CH '48?

AB '48. Oh yes she was at the university zoological laboratory during the war but I don't know really, I'm not familiar with everything there. I mean Otto Lous Mohr was arrested. He was for some time at Grene [?] Prison.

CH Wasn't he sent to Berlin though?

AB No. that was the Rector, [Sait][?] I think he was sent to Germany but not in a concentration camp. That was

CH That was Keppler.

AB And probably because of some family relations which really managed to put him somewhere else. But Lous Mohr, I don't know how long he was, because at a certain moment they arrested a lot of the Professors from the University. My grandfather was there for I think at least, almost a year I think, so the university was in some respects not working, but of course they had put all the Nazi academics in there. Klaus Hansen was it?

CH Yes. He was in the Department of Anatomy actually with Mohr, Klaus

Hansen.

AB Ah. Yes. Is that right?

PH Did this cause a big problem at the end of the war, as in some other countries, in terms of some polarisation between those academics who had collaborated and those who had not? How was this resolved?

CH They were imprisoned, the collaborators, or put in detention after the war.

AB They probably got some months or years of prison, a lot of them.

PH Because one of the things which of course I came across in Germany was that, very much in this process, after some time, the same people were then put back in their old posts and carried on doing the same kind of work, which caused huge later problems . .

AB I think the situation was different in Germany, because I think there weren't many, let's say, geneticists opposing the Nazi system, so that was quite different I think in Norway, where most of the people were against everything, so the Nazi party in Norway was a very small party all the time.

PH Just coming back to Scandinavian cytogenetics again, when did prenatal diagnosis first start to develop?

CH I can tell you that exactly. I told you the story and it started actually, we started to grow amniotic fluid cells in 1970 and did some work on that before 1970. And then we had the first challenge in December 1970 and then in January, about the 10th or 15th January, at a winter meeting, and I was dancing with Annelise Börreson.

AB Yes, I remember her.

CH And she had just graduated in December as a biochemist and had nothing to do, and I suggested that she should come and work with us and try to establish the prenatal diagnosis in an actual patient, so we did that.

PH That's quite unusual, because in most countries cytogenetic prenatal diagnosis came before any biochemical.

CH We did grow cells and leukaemia chromosomes.

AB You did cytogenetics and she was trying to do the biochemistry.

CH The first diagnostic was not cytogenetics, that was actually biochemical.

PH Did you have much contact with the people in Copenhagen, for instance I had a short note from Povl Riis who had looked at amniotic cells, I think really using sex chromatin?

AB That's right. That's was the first I think in Scandinavia.

PH Along with Fritz Fuchs. He has written a short note for this historical series and I wondered whether there was much connection between the different units.

CH No no, there wasn't. We had no connection with . . .

AB Because Jan Mohr at the time was Professor in Copenhagen from '64, and then Kåre Berg came in '67 and in the meantime, actually he was in charge of some of our institute in Oslo, and I used to say we had been under Denmark for four hundred years and it worked, with much lousy communications. It worked and this was because he wanted all the young people that we could most of the time, for our dissertations, for the degree, so he put his name on all the bills and so on, and came up every second month or something I think.

PH So was there quite a a long interval between Jan Mohr moving to Copenhagen and Kåre Berg?

AB Three years, from '64 to '67.

PH Three years. Why was it so long an interval?

CH I don't think Jan had actually decided to stay in Copenhagen at the beginning, but I don't know that for sure.

AB That's possible, and there was a delay at the University to announce that there was a professorship, so Kåre Berg could apply

CH Then it was not a full professorship with Jan.

AB No, he was an associate professor.

CH So it took some time to actually establish.

AB I think that was the reason why they took 3 years.

PH That's very interesting. Are there any other steps you feel I ought to know about and document, for the people outside Norway, that we haven't talked about?

AB Of course we had a lot of collaborations with the people at Jan Mohr's Institute like Margaretha Mikkelson. And then of course with Helsinki with Albert de la Chapelle. He also did his thesis on cytogenetics. So he was cytogenetics in the beginning. And then also rather early there was a cytogenetics laboratory established in Bergen with

CH Aarskog

AB Aarskog

CH He claims he started that in ’61 or so.

AB Something like that.

PH Is this the same Aarskog as the syndrome?

CH Aarskog syndrome, yes.

AB That’s him. Paediatrician actually he was.

CH He had some cytogenetics training as a paediatrician, in Edinburgh or at least UK.

AB Yes, I think with Bergen, they had a closer connection with England, that’s why he had a link with the people in Edinburgh.

PH Tell me just a little bit about Margaretha Mikkelson because she was one of the people I was hoping to interview, but was not able to before she died, so it was a great loss.

AB Oh sure.

PH And I didn’t like to ask Jan Mohr, because I knew there was some difficulty.

AB That’s right. They didn’t co-operate very well and I think she moved out rather early after Jan was arriving, and got her position with the . . .

CH Kennedy.

AB The Kennedy Institute, where she run a huge laboratory for cytogenetics, in particular in relation to Down’s syndrome and other types of mental retardation.

PH So would I be right in thinking that in terms of clinical cytogenetics, would it be fair to say that most of the development occurred at Kennedy rather than at Jan Mohr’s Institute?

AB I think that would be correct. And there was of course at Rijkshospital in Copenhagen, there was John Phillip who was doing cytogenetics. He was a gynaecologist. So he did I think a lot of studies with

CH Amniotic fluid cells.

AB Sex deviations of some sort, but I don’t know whether he really continued with this. Of course I lost track of all these things because I moved from Kåre Berg in ’69 to the Radium Hospital, and so I changed my subject completely, worked with carcinogenic substances and chromosome aberrations. That was quite different. And then of course we, rather late, did anything with cancer chromosomes. That was actually much later.

CH Events. I think its fair to say we talked about that, the establishment of medical genetics as a speciality in the Medical Society. That was in ’72. It was an early one.

PH Very early.

CH and establishing the requirements for claiming such a speciality from the beginning.

PH When I was speaking with Kåre Berg, he felt that probably Norway was the first country in the world to have medical genetics as a full specialty. And I think he was probably right.

AB That was something like

CH ‘72

AB ’72 already. I see.

PH Well, thank you both very much. I think I will finish it there. It’s nice to see you.