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Victor McKusick Oral History

Victor McKusick

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Susan Mehrtens' Note: Victor McKusick has been both a Trustee of the Lab and founder of the annual "short course" in genetics that, after 27 continuous years, has become a Jax tradition. A professor at Johns Hopkins, McKusick first developed the "short course" with John Fuller, and with Earl Green's encouragement. It is obvious, from this interview, that the course is an integral part of McKusick's life. Certainly it was about the only he discussed during our taping. The interview speaks for itself about the course, its history and purpose. The interview does not speak much at all to the assessments McKusick might have made regarding his role as a Trustee, the Lab's current situation, the three Directors he has worked with, etc. As it stands, this tape and interview provide the best description of the "short course" in this collection.

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The Jackson Laboratory
Oral History Collection

Interviewer's Comments

Narrator's Name Dr. Victor McKusick

Interviewer's observations about the interview setting, physical description of the narrator, comments on narrator's veracity and accuracy, and candid assessment of the historical value of the memoir.

NOTE: Use parentheses () to enclose any words, phrases or sentences that should be regarded as confidential.

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14 July 1986

Date

Susan Mehrtens

Interviewer's name

Oral History Collection

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Place Mt Desert

Date July 14, 1986

Victor G. McKersie
Narrator

Susan McIntire
for the Laboratory

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Narrator's Name McKusick

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- 2.
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- 10.

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Interviewer's Notes and Word List
Dr. Victor McKusick

Chai Cottage
Earl Green
Baltimore
Johns Hopkins
Piscataquis
Vincent
Testa's
John Fuller
Lucille P. Markey
Mount Desert
Jackson
Saco
Lewiston
Portland
Aroostock
Melba Wilson
Tom Roderick
Oakes Center
Atlantic Oakes
Bowdoin College
Sir Harry Oakes
Emerson School
C.C. Little
Bar Harbor
Egypt
Perth, Australia
Boston
Rich Prehn
Barbara Sanford
Gramm Rudman
Ken Pagan
England
California
Dr. Snell
Nancy Ruddle
Toronto
Margaret Green
Hamilton Station
Sawin

Terms:
linkage
somatic cell hybridization
cystic fibrosis
hemophila
muscular dystrophy
cytogenetics
phenotypes
homologous
histocompatibility complex
HLA
H-2

This is the tape of an oral history interview of Dr. Victor McKusick, given as part of the Jackson Laboratory Oral History project, sponsored by the Acadia Institute. This interview was held on July 14, 1986, at the Chai cottage on Long Pond, in Mount Desert, Maine. The interviewer was Dr. Susan E. Mehrtens.

SM: Why don't I begin by asking you how you first heard about the Jackson Lab, and how you wound up coming here?

VM: I first came here with my wife in the summer of 1959, on the invitation of Earl Green, who then was Director of the Jackson Laboratory. Dr. Green had visited us in Baltimore, at Johns Hopkins Hospital, as part of a site visit, on an NIH grant application that had to do with studying linkage in man, and this was in January of 1959. He knew that I came from Maine, and suggested that I ought to visit the Jackson Laboratory because of the comparable type of work in linkage that they do in mice. Of course, my linkage studies were in man.

I was born and brought up upstate, in Piscataquis County, but had never been to Bar Harbor, in fact, until the time I visited the Jackson Laboratory in 1959. I knew about the Jackson Laboratory. As you may know, my identical twin brother, Vincent, is Chief Justice of the State Supreme Court here in Maine Court here in Maine, and I have many relatives here in Maine. So we visited here, and the idea for a course was conceived during that visit. I always say, and, if you come to my illustrated history of the Bar Harbor course on Thursday evening, you'll hear me say it

then that the course was conceived at Testa's Restaurant on a warm July mid-day. We were having lunch with John Fuller, who, at that time, was Assistant Director for Training at the Laboratory. I suggested to him that there should be a course in medical genetics up here, for medical school faculty people, in particular. The Jackson Laboratory people had much to teach us in medicine because of the rather parallel things that they do in mice. Mainly they identify, from phenodeviant mice, mice with mutants of one type or another, and then go on to try to figure out how it's inherited and what the nature of the basic biochemical defect is, and what the linkage relationships are, and so on. At that time, both teaching and research in medical genetics were in a very primitive state. The course was designed primarily to teach the teachers; to upgrade the teaching of genetics in medical schools, and related professional schools, such as dental schools, even veterinary schools, and, to some extent, to teach teachers of human genetics at the university level. A secondary, but very important objective was to upgrade research in this area by exposing the "students" to the availability of mouse models, for example, as well as to concepts of genetics useful in their research.

So, the idea went through a gestational period of one year, during which time we acquired financial support from the National Foundation March of Dimes, nee National Foundation of Infantile

Paralysis, which had just, at that time, 1958 to be precise, was broaden its objectives. The organization was looking around for new worlds to conquer, so they went into the field of arthritis and the field of birth defects. A few years after that, they gave up arthritis, and limited themselves to birth defects. But they were agreeable to supporting the course, and continue to do so to the present time. Their grant for the support of the course is the longest standing grant in their entire history. Until a couple years ago, they were the exclusive supporters, financial support, for the course. Other support from the NIH and from the Lucille P. Markey Charitable Trust has been added in recent times, as well as a contribution from private donors, but the March of Dimes has been in there from the beginning, at least to some extent. The Course, from the beginning, had a wide representation of people as "students." In the early years in particular, they were largely medical school faculty people, many of them very senior people--department chairmen and full professors in abundance, and at times even a Dean or two, who would be concerned about what their school should be doing in the area of genetics. In recent years an increasing number of people have been more junior postdocs even some pre-docs. These people have been a very exciting group to have, along with the older group, which is still well represented. I don't know how much you want me to tell you at

this time about the evolution of the course, but I can tell you how the course has evolved. This is the 27th year of the course. It was first given in 1960. Human genetics itself has evolved tremendously and medical genetics has evolved tremendously over that period. There's been a very valuable mutual strengthening in this country, of human genetics and mouse genetics, and of the programs of the Jackson Laboratory, as a result of this interaction, that takes place every year. The course is put on by a group of us from Johns Hopkins, which for quite a number of years now has numbered about 12; a group from the staff of the Jackson Laboratory, which numbers also about 12; and then a group of guest lecturers from other institutions, which numbers about 12. So we have a very high student-faculty ratio. The group of guest lecturers turn over about 75% each year; this permits us to bring in very exciting people. We have insisted from the beginning that this is a course, not another symposium, seminar, or conference. This means that we cover the entire waterfront, and start from first principles. This does not mean, however, that we don't go into great depth, and it doesn't mean that we don't present very exciting new stuff every year. Even though we emphasize to the lecturers that they shouldn't do too much "seminaring", that this is a didactic course, we encourage them nonetheless to interject the latest discoveries, to use as example materials

from their current work in the laboratory or in population groups or the clinic. As far as the Jackson Laboratory is concerned, it's rather interesting that from 1960 through 1966, this was a medical genetics course. It was called "A Short Course in Medical Genetics." Then, beginning in 1967, in odd numbered years, it was called "A Short Course in Experimental Mammalian Genetics," mainly mouse genetics. That was true from '67 through '77. This seemed desirable because the mouse tended to get short shrift in contrast to human genetics, and the approaches were somewhat different at that time. In 1979, by good rights, it would have been a mouse course, but 1979 was the 50th Anniversary of the Jackson Laboratory, as you know, and it seemed desirable, for that reason, to have a human course as well, so we had a combined course in 1979, and it's been combined ever since. It's been called "A Short Course in Medical and Experimental Mammalian Genetics" because what has happened --and I think the Course and the interactions between the mouse and human genetics contributed to this--what has happened is a convergence of mouse genetics and human genetics. The convergence is in large part also because of the development of so-called parasexual or surrogate methods of studying human genetics, such as somatic cell hybridization, and such as molecular genetics methods going directly to DNA itself. These methods are equally applicable to mouse and to man. This year, it seems to me that the integration of mouse

and man has been particularly impressive, that the lecturers move easily back and forth between mouse and man. You hardly remember that you're talking about one species, rather than the other. The mouse, as the most studied mammal, from the genetic point of view, is terribly important as a model.

Do you ...

SM: What?

VM: Do you ...

SM: No. I have a... (laughter) Now, how did the Jax, aside from the staff--I know the Jax provides the space--how else do they sponsor the Course, or, I guess, that's all they have to do.

VM: They have marvelous library facilities and they provide this marvelous Mount Desert setting which is hard to beat, and of course is important to the success of the course. A very pleasant setting in which to have our coffee breaks encourages exchange among the students and faculty at that time. The trails and other recreational activities get people mixed up. Lots of scientific collaborations have had their start at this course--collaborations with some of the Jackson people using mouse models of diseases that the people who come here as students have as their main focus of interest. Among the student body, collaborations have been initiated because of the acquaintances that are made here in the course. In a way of the contributions of the Jackson Laboratory

are more substantial than the contributions of Johns Hopkins, because we bring only intellectual equipment along here, and the Jackson has the physical facilities to contribute. We have, during the second week, a so-called Mouse Clinic, which is tomorrow morning, at which a great variety of mouse mutants are presented with discussion of how these can be put to use for studying human disease, and then now for a long time, we have also had a Medical Genetics Clinic. We have patients who come from eastern Maine, or all over Maine, from Saco, Lewiston, Portland area, up to Aroostook County--all over the place, and some of the summer people who are up here, who have various hereditary disease problems, they come both to consult the doctors who are up here, and also, with their permission, to be discussed in connection with the conference. So we have patients with cystic fibrosis, or muscular dystrophy, or hemophilia. We can discuss them both from a clinical point of view, and from a genetics point of view. For the families, the quid pro quo for this, is genetic counseling and often advice about specific clinical problems arising out of their genetic disease, so this has been a very valuable part of what Johns Hopkins has been able to contribute. The Medical Genetics Clinic is organized mainly by the Center for Human Genetics that Melba Wilson runs. Tom Roderick has been key in getting the Center organized, as have also some of the M.D.s in this area.

SM: How long does the course run?

VM: Two weeks.

SM: It's quite intensive then.

VM: Very intensive. We have 4 hours in the morning, minus a half-hour coffee break, and then in the evening, we come back at 7:30 and go for at least an hour and a half, often longer than that. It used to be, in the earlier years of the course, that the afternoons were free for recreational activities, but we have introduced optional workshops, which are taken by the majority of the students. We have workshops in cytogenetics, biochemical screening, molecular genetics, and methods of linkage analysis, and starting last year, we initiated a workshop in computer methods of handling genetic information, which goes all the way from DNA sequences up to syndrome identification.

SM: How do you pick your students? How do you pick people who are...?

VM: Well, they pick themselves, to a large extent, but we have more applicants than we can accommodate, so we really judge whether they are people that will use the information to the best advantage. We like to have people who are on university faculties, because we do like to "teach the teachers". We can't accommodate more than a certain number. The first two years, it will interest you to know,

it was given at the Oakes Center, which you now know as the Atlantic Oakes.

SM: Oh my goodness!

VM: The Oakes Center belonged to Bowdoin College at that time. It had been a summer home of Sir Harry Oakes, who was murdered down in Nassau, as you may remember, and it was run as a conference center by Bowdoin College. Subsequently, of course, Bowdoin found it unprofitable to keep up, and sold it, for its present role as a motel/hotel. That was an interesting place for the course for the first two years, and then we moved to the Emerson School, when it was built, and we were there until 1973. From 1962 until 1973, inclusive, we were at the Emerson School, and then the conference center/library center named for C.C. Little was built at the Jackson Laboratory, and we've been there beginning in 1973.

SM: How many students do you have, about?

VM: I started to tell you that the first year, we had 45, I believe, and that was determined by the limit of space at the Oakes Center, and then the second year, we went up to 63 or 64. This year's our largest group yet. We've been over a hundred for a long time, and we're up to, we accepted about 127, and our Auditorium holds only 126, and we have a big faculty, as you know, too, but we have put a closed-circuit television in the foyer there, so we can accommodate the over-flow, and we always have a certain number of last minute cancellations. This year, we've been crowded, but not uncom-

fortably so--

SM: How many of these people continue to maintain contact with the Lab, do you have any idea, that take the course, that develop a collaboration?

VM: I couldn't give any precise figures, and the proportion would be, would seem like a rather small figure, but it's a very significant figure. Every year there is a fair number that establish contacts that continue. We have some repeaters in the Course. We have so many applicants that we don't feel we can accommodate too many of those, but the Course has gone on long enough so that many people feel that they need a retraining after ten years or so.

SM: I would think.

VM: We also have quite a lot of students from abroad through the years. Some of these are people who have been in this country doing post-docs or fellowships of some kind, and before they go home, have taken the Bar Harbor Course, but others have come to us directly from Europe for the course. This year we have a woman from Egypt, someone from Denmark, someone from Perth, Australia. In fact, we have two people from Australia. I don't know where the second person is from. We have someone from India, someone from Holland.

SM: Wonderful. Did you at any time begin to think the Jackson Laboratory was getting stale, in the sense of out of touch with the forefront of genetics? I ask that question because

several people I've interviewed wondered in their emphasis on classical mammalian genetics if some of the molecular stuff wasn't sort of getting...

VM: I think they have come into the molecular age very effectively in recent times. I do think that the course has contributed to this rubbing elbows, not only with faculty people but also with the students from many different institutions, has been terribly beneficial toward broadening the horizons of the staff of the Jackson Laboratory, and I'm sure that their research interests and activities have been widened as a result. It's hard to speculate about what would have happened if this course had not been going on for these 27 years, but I think that the Jackson Laboratory would be quite different, and I think less advanced institution. They've gotten some very good young molecular geneticists in recent times, and some of the old-timers are working on much the same problems they were before, but bringing molecular genetics to bear on their problems.

SM: When you were first approached about teaching this course, what--

VM: I wasn't approached, of course: We conceived of it and we jointly, John Fuller and I, with the very strong endorsement of Earl Green, got it started.

SM: What was your impression of the Jackson Lab, or what did you think its reputation was?

VM: Oh, I had a very high regard for the Jackson Lab. I thought this was a phenomenal place.

Like me, they were very much interested in all of hereditary disease, and it impressed me that they were doing in mice just the same thing we do in medical genetics: You identify abnormal phenotypes, and try to figure out, in the first place, if it is a genetic disorder and then, in the second place, how it's homologous to disorders in man, and in the third place, what the basic defect is, and so on. They had found muscular dystrophy in mice that had promise of being the same as a form of muscular dystrophy in man. This was a very exciting sort of approach. Also, I've always been interested in mapping, and it's impressed me what great advances in mouse chromosome mapping they had been able to make here, in contrast to what we were able to do in man up until about ten years ago.

SM: They've just come out with a new gene map of the mouse.

VM: Yes. This was handed out at the course.

SM: Now when you actually teach this course, do you confer before the course begins with your fellow teachers at the Lab?

VM: Oh yes. I was up here--I'm on the Board of Governing Trustees of the Lab, so it sort of gives me an excuse to come up here for a period to work on the Course too, but I was up here in October to get started on whom we were going to the course for this year, and how we would organize the Course for this year, and then there was another meeting

of the Trustees in Boston in April, and I came up for that, and Tom Roderick, who's the co-director of the Course came down from here, and then we did a lot of telephoning back and forth. Then, aside from that, I convened my group at Hopkins, and he convened his staff up here, to get suggestions, and then we compared notes.

SM: How long have you been a Trustee of the Lab?

VM: I was on the bigger board before--since '79, or something like that. I've been on the Governing Trustees Board for two or three years, I guess.

SM: It's a lot of responsibility, and involves a lot of travel, I guess.

VM: It hasn't been too onerous, really.

SM: Do you remember any interesting anecdotes or funny incidents involved in all these years of teaching the course?

VM: Yes, there are lots of things related to the personalities of individuals from the faculty or the student body. It's hard to think of many people in human genetics or in mouse genetics in this country, or indeed to a considerable extent elsewhere, who haven't either been students of the Course or members of the faculty of the Course, and oftentimes, both. We have many examples of people who were students of the course and later came back as members of the faculty.

SM: That's good. Have you seen changes in the Jackson Lab? You've seen now three Directors, I gather: Earl Green,

and Rich Prehn and Barbara Sanford.

VM: Yes, and it was pleasant to get to know C.C. Little a little bit, so I have known all--

SM: Oh, you have known all--

VM: I have known all the Directors. I used to see Little only socially, really, but when Earl Green was Director, he always had a party every year. Our sessions are Monday through Friday, and on Saturday morning, and then on Saturday afternoon and Sunday we're off, ... and Dr. Green always had a party at his house on Saturday afternoon, and he would invite the entire staff of the Jackson Laboratory, and retirees, and people from the Mt. Desert Island Biological Laboratory. It was always nice to see Dr. Little on those occasions but I can't say that I knew him well. The Prehn era is sort of an unfortunate time, in many ways, of course, and he was just a misfit there, as it turned out. I don't know that anyone predicted that. I wasn't in on the recruitment of him, but as it turned out, he was not for the job, so it seemed. I'm tremendously impressed with Barbara, and I think she's been just the person the Laboratory has needed, and has worked out very well.

SM: As the federal government begins to cut back in terms of financing, with Gramm-Rudman and all that stuff, what do you think is going to happen in terms of Lab funding and programs? Do you think they will just pick up private donors now?

VM: I think it's very serious problem. I also hear from Ken Pagan, in California, and also in Europe and England, in particular, that the Animal Rights movement has had some undesirable effects on the use of mice in research, as surprising as that may seem. Such things always start in California, I guess, but England has a very strong Animal Rights movement, as you know.

SM: My goodness.

VM: So, that is something that is a little bit worrisome, both from the point of view of the use of mice in research that might reflect itself on the production side of the Lab, which is very important to the support of the whole operation, and also on the conduct of the research itself here.

SM: Right. When you look back on the activities of the Lab, what do you think have been its major discoveries or contributions to science?

VM: Well, one thinks immediately, of course, of the major histocompatibility complex, H-2, and the Nobel committee obviously thought that was outstanding, giving the Nobel Prize to Dr. Snell... that's way out in front. That's one instance where you can pick out something that has been helpful. HLA, the human counterpart of H-2, was sort of coattailed on H-2: H-2 really led the way to a tremendous extent. So often the question you asked can't be answered in terms of some really tremendous

landmark such as that. It's a bit like talking to Nancy Ruddle, who's just returned from Toronto and the International Immunology Congress. When you get back from a World Congress, people say "What was the main thing at the Congress?" and so often, it's a superb conference but there isn't one thing--it's an aggregation of many small things, or the bringing together of a lot of loose ends that have been sitting around in a frayed state for a long time. And I think that's true of the contribution of the Jackson Laboratory, that there aren't very many H-2's, but in the aggregate, there are so many things that they have contributed to. Perhaps in a generic sense, mouse models is one very important thing that one can point to. The neurological mutants have been very important to both the analysis of how the nervous system develops, by studying how it goes awry in these mutants, and also, very important from the standpoint of homologous human diseases.

SM: Some of the scientists have said they have mice they named "weaver" and "lurcher"--all these funny names they have.

VM: ... "waltzer"...

SM: Strange, interesting names. Have you ever done research at the Lab for any length of time yourself?

VM: No. In 1968, we stayed up here and did some gene-hunting... looking at families with various

hereditary traits, on Deer Isle and elsewhere in eastern Maine, but I don't work with mice at all. I always participate actively in the planning of the Mouse Clinic, discussing possible homologous conditions in man, in relation to mouse mutants, and I always have lots of questions for people like Margaret Green when I come up here, to see whether such and such a mouse mutant has relevance to a human disease, but as far as doing any hands-on research with mice, I don't.

SM: Have you seen any change in the mission or identity of the Lab over the years you've been here? It's obvious it's changed its physical identity: They have a nice conference center now. Do you see any other change?

VM: I think the emphasis has remained about the same. I think there has been remarkably little deviation from the interest in cancer and genetics.

SM: Do you think their bringing molecular geneticists on to their staff has changed that some, or is that just intensifying the--

VM: No. I think it's just an addition of a new and powerful methodology to the old problems. It's just that it has enhanced their approaches to the same problems and toward the same goals.

SM: What do you think the Lab's weaknesses are, as an outsider who sort of has a foot in the place?

VM: I think that it would be nice, of course, if their funding was a little more secure. It would always be desirable

if they had an substantial endowment and I think that probably they have some problem in recruitment because they are competing with much better-heeled institutions. The relative isolation is both an advantage and a disadvantage. For many people, I'm sure, it comes out on the negative side. It may be that--I'm not certain that they get the very best graduate students to work, and that, of course--they're a research institute, and not an educational institution, but they do, of course, get people who are doing their doctoral theses with--and they have a good many post-docs, and I'm not certain that they attract the very best people perhaps, in either of those two categories. But all of these are relative weaknesses, so obviously they are not a complete black eye.

SM: Have you ever sent a student to work under someone at the Lab?

VM: Rarely. I had a girl who did a Ph.D. thesis on the genetics of hand malformations, and she spent a very profitable time up here, reviewing limb malformations in both mice and rabbits. They had rabbits at that time. As you know, there was a time when there was some dog research going on here, at the so-called Hamilton Station, out on Route 3. There was a farm out there that was subsequently sold where they had a dog colony, and the purpose, the idea, was to study behavioral traits, the genetics of behavioral traits, in particular, and they also had quite a lot of rabbit

research going on, and John Fuller, whom I mentioned earlier, was involved in the dog research to quite an extent. Paul Sawin, a leading rabbit geneticist, was here for quite a long time, and kept the rabbit colony.

END OF SIDE ONE

...Everything was closed out except the ... mouse.

SM: ... much more on mice.

VM: Yes.

SM: Would you say that the values that drive the Jackson Laboratory are basically scientific? I ask this question because some people have wondered to me whether the mouse production, at least to the Trustees anyway, doesn't sometimes overpower the science, because after all, the mouse production brings in a nice healthy black bottom line, and the science--it's really hard to say: Now, what does that mean? Have you ever thought that there might be this strain between the two of them?

VM: You know, I'm a Professor of Medicine, and was Physician in Chief of the Johns Hopkins Hospital for 12 years, and this same thing goes on in academic medical centers, that the Boards of Trustees and administrations often have a different view of what hospitals should be and should be doing than do the people on the academic side, and so I feel that's an issue. The Jackson Laboratory, of course, including its production facility, as far as I know, is tax-exempt

and then, of course, if it weren't for the research, it would not be a tax-exempt institution and they have been under fire some times in the past, as far as their tax-exempt status. I think some of the citizenry of the state has questioned the appropriateness of that, which I of course don't have any doubt about, but if it weren't for the research, there wouldn't be any justification for production, as a tax-exempt function. Of course, the Laboratory, was founded just as the Crash was occurring, and they had a terribly hard time making ends meet during the Depression, and the sale of mice was one of the ways they evolved to keep their head above water, and it still is terribly important to the functioning of the Lab. The connection with the production facility, they keep a very close eye on the breeding stock and what the breeding stock produces, for reasons of quality control, but also they keep a very close eye on it for any new mutations that come out that may be very interesting, previously unknown ones, which again may be very valuable models for human disease--so that's one research aspect of the production. Rather than just making money, it is a very valuable service to the scientific community, and it turns up many mutations.

SM: Someone explained to me--maybe it was even Earl Green--that you wouldn't get these numbers of mutations if you didn't have a sizeable colony, and when they were approached about this tax-exempt business, they were able to make a

convincing case to the IRS that they needed millions of mice because that's how you get mutations in any kind of number.

VM: Yes.

SM: And they bought it.

VM: Yes.

SM: Have you ever worked with young people? I know they have a summer students' program for young people, but your course doesn't involve them at all.

VM: No. Many of them sit in on some parts of the course, and sometimes, my wife, who is a physician also, talks to them, but I do no actual teaching specifically related to them.

SM: It sounds like it's a really high-powered course, with that faculty like you have.

VM: Yes. And as intensive as it is.

SM: Now, on Thursday, you're going to give a retrospective?

VM: Yes.

SM: Do you do this every year?

VM: Yes.

SM: Is it at 7:30 or 8:30?

VM: It will be a 9...There is a regular--No, I think it is at 8:30. Yes. There is a lecture on prenatal diagnosis 7:30-8:30.

END OF INTERVIEW