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Professor Kenneth Reid FRS in interview with Dr Max Blythe
Oxford, 28th January 1997, Interview I Part One

MB Professor Kenneth Reid, you were born in Peterhead, way out in the east of Scotland, in 1943.

KR That's right, yes.

MB It really is, I mean that really is north, north-east.

KR Most, the most north-easterly point in Scotland.

MB Yes. And it was a, it was a small town, fishing town?

KR It, was … famous for fishing in the early century and in the 1800s it was a, it was a whaling centre.

MB Right.

KR And then the, in the era of the herring fishing it was very big in terms of catches of herring.

MB Looks as thought it might have been a bit cut off in the old forties there. I mean, when you first remembered it. I mean, was it a bit cut-off, a community out, outside…

KR It's, it's slightly isolated and it was originally famous for its prison of course, because it was set very close to the North Sea. And then, in the sixties and seventies with the oil and gas developments, the oil and gas lines came in and changed the character of the town quite dramatically. It went from ten thousand population to over twenty thousand in about ten years, so you can imagine it…

MB But it was about ten thousand when you were a boy?

KR Yes, yes it was.

MB You must have felt that you really knew that kind of size of a town, been very home … you know, at home there.

KR Oh, yes, I think, you know…

MB Ken, I want to take you through that part of your life, that early phase – talk about parents, what it was like living in that town, a little bit more, and the kind of schools you went to. So perhaps you could start with parents.

KR My…

MB Your father was in business?

KR My father, my father had an accountant's office in the centre of the town. And my mother taught domestic science. She was a teacher in the various schools in Peterhead and she did a, she took a degree at Edinburgh, a place called Athol Crescent. And that was one of the best places apparently in those days to do this type of teaching.

MB So it was a professional family?

KR Yes.

MB But you said you had farming, you'd had farming and business roots.

KR My mother, her mother and father were very much sort of farming stock. My grandfather was a butcher and he owned a, quite a large bit of land out, just outside Peterhead which was farming land. And … the, I can remember, in fact I was born there in, in '43, and spent my first few years on, on the farm, and then only moved into Peterhead sort of early life.

MB Right, so kind of rural beginnings, and then a townie. And that period in which you were growing up, you know, was just post-war – I suppose you remember that kind of rationing phase. But there can't have been much rationing for a, for a butcher's family, in the farming world.

KR Well, farming contacts and the farming community – I suppose we didn't have as many problems as others, but I can certainly remember rationing … for sweets and other things, I mean…

MB Did your father have his own business though, in the town?

KR Yes, he … had a, quite a large accountant's office, which thrived and… He kept on the business even after he retired in '65, and it kept, he just moved it into our house, which was fairly large. He'd built an extension to that, and…

MB Still continued people's books…

KR He just continued working until he died! He didn't envisage fully retiring.

MB You weren't the only child?

KR No, there were four of us. I had a brother who was, still have a brother who's five years older, a sister who's three years older, and a sister who's five years younger.

MB Right.

KR So they spread us out over quite a … wide…

MB It was a close family?

KR Yes. Uh-huh.

MB Kind of took holidays together and spent a lot of time together.

KR Yes. Mm-hmm.

MB Just trying to think of early memories, what you, what you might remember of those post-war years – the early memories, in that town.

KR Mmm, I suppose it was a rather sleepy town… I suppose my childhood memories have all been there … a long, around the long summer holidays. And, although it was a town in the north-east of Scotland one of my favourite pastimes was playing tennis – I spent most of my summers playing tennis or playing out in the, in the farms, and walking round the coast. That was my…

MB But that wasn't until you'd started school – we haven't, we haven't quite got you there yet, so we're, we're running a bit ahead. Did, I think you said very early on you remember the kind of fog-hooting going over the harbour…

KR That was a feature of Peterhead – its … weather conditions were quite harsh. And in the summer you would have beautiful sunshine half a mile inland, but the whole town would be shrouded in fog, and this foghorn going all day and all night.

MB So you heard this as you're retreating into sleep. Ken, we'll just take a look at the, the family a little bit more. You've talked of a brother who was a bit ahead – I guess he was too far ahead to really be influential.

KR Well five years is quite a big difference of … he was eighteen when I was thirteen. He went to university first, obviously, and he did an, an honours degree in psychology at Aberdeen University, so it was a, sort of…

MB He got a first, I think.

KR Yes, he got a first class degree – sort of set the sights for the rest of the family. And I suppose we, as a family we never thought of doing anything else but higher education, which I suppose was very good in a way, and…

MB But when you went to school, it didn't start out all that well.

KR No, I had an unfortunate … start. When I was four to five years old, apparently I had a hearing defect which people didn't realise. And the first year of schooling the teacher sort of brought my mother aside, about after six months, and said 'Well it's a pity about poor Kenneth. He doesn't seem to appreciate what's going on.' And apparently there was a, at school they would put the … the not so bright students were put to, further to the back of the class!

MB A great help!

KR Apparently I wasn't hearing anything at all! So my first six months of schooling were a bit of a waste of time, and… But after that it was seen to, and I was sitting at the front of the class, so that seemed to help me.

MB Did that have an affect on your confidence? Did it undermine you?

KR I think it, I think it probably did, because I can certainly remember very little about my first year at school, and my second and third years I think I did struggle. And it wasn't until I reached the sort of ten/eleven stage, and there was a, the exam called the eleven-plus when you went from primary school to secondary school, they, they started to…

MB Oh, the exam for Peterhead Academy was it?

KR Peterhead Academy, that's right, and…

MB Yes. And then you did rather well.

KR Yes, I had great encouragement from the headmaster of the primary school.

MB Who was he? Let's put him on the record.

KR Stanley Martin, who was headmaster of St Peter's Episcopal School. And he encouraged me, and…

MB Did he actually teach?

KR He did teach.

MB He wasn't, he wasn't just an administrator?

KR He was head of the school but he took the final year class…

MB Right.

KR …full-time. So as well as the administrative work he was teaching full-time.

MB Pushed you a bit, did he? Was he a, I mean…

KR He was, he was very good at encouraging people and pushing people forward.

MB And so you, you found yourself then – at that, at that kind of stage you began to feel that there was a future in education?

KR Oh yes, and I think, due to his influence I think I did…

MB He was the main instigator of that period?

KR …I did quite well in these examinations and made it to the top class in the secondary school, which was again important to get a good start in secondary education.

MB Yes, because you didn't divide schools – you went to the same school but you were put into different layers.

KR Yes, the secondary schooling in Peterhead, it was quite a large academy, it was … seven, seven or eight hundred I think at that time…

MB Right.

KR …and was getting on to a thousand by the time I left. Because they, they took in pupils for secondary schooling from all the farming areas, and all the communities round about Peterhead. And they divided the classes into the, what they called the C classes and the T classes – classical and technical. So there was a clear division even then which I think, I think with hindsight was a bit harsh, and streamed people off too early.

MB Yeah, very early. Before you do that, let's just stay with those early years before eleven-plus kind of exams arrived. You were a cub – you got involved in cubs and did quite a lot with that?

KR Yes, I joined the cubs, I think probably at the age of five or six. And … I joined that and went on from the cubs to the scouts. And that was part of my memories of childhood, going on these scout camps, because the, we would go to various parts of Aberdeenshire, a bit beyond, spend a week in tents and… And that was one of the highlights of the summer holidays.

MB And was that a lot of, a lot of hill walking?

KR It was more supposed to teach you how to interact with other people and a bit of discipline. There wasn't a lot of hiking.

MB I just wondered, because you are a great hill-walker nowadays, whether…

KR Whether it did stimulate my interest in walking.

MB Ken, just keeping to that kind of leisure in those early years – did you go to the farm a lot? Did you have holidays there? Was that one of…

KR Yes.

MB …a permanent part of that early life?

KR When we were younger, as a family we didn't all go, say to, abroad – America, Europe. I think that wasn't the usual thing in the fifties. For, because although my father was well off I don't think he was that well off! And we would often go to relatives and stay for a couple of weeks on the farm, which was quite a change of course from staying in the, in the town.

MB That home in which you lived … it was, it was fascinatingly a hard working one. I mean, you really all had your heads down at one of the… Is that right?

KR Yes. Well, my mother was bringing up four children, so she didn't get back to full-time teaching until I suppose my youngest sister was back in, doing her secondary schooling. So, she had a fair break from full-time teaching, although she'd managed to do some part-time.

MB And a kind of symbol of the times you've, you talked at one time of sometimes having to move out of a room because it was so smoky. Because there was a lot of smoking there – both parents smoked quite a lot.

KR I did, well my father was a chain-smoker and my mother smoked a lot, and I think this, this influenced the children, yes…

MB But the dangers hadn't been written at that stage, had they, they were…

KR No – I think it's a bit sad that they didn't appreciate…

MB Because they both paid a price for that smoking?

KR They both ruined their health, and my mother died of lung cancer and my father also died of cancer.

MB Ken, take me now to Peterhead Academy. What was that like? Was that a culture shock or was it just a steady progression?

KR It was quite a difference from the St Peter's Episcopal School's rather small, insular little school to move to this academy of seven/eight hundred people. It was a big shock, and I found the first year very tough because, just the sheer numbers and the pace of things. But, in the end I quite enjoyed my schooldays.

MB There were a few early up and downs, but you stabilised in a fairly, in a fairly high form, and had a classical, fairly highly pressurised education early on?

KR I did Latin and French and physics and chemistry and maths and English and history. These were the main subjects I did, and these were the subjects I sat for the so-called 'Lowers' and 'Highers' which were, the great Highers were the grades you needed to get to university.

MB Ken you mentioned, just, I'm just flicking back a moment, you mentioned that St Peter's Episcopal School… I'll just, I'll just take that in for a moment, because I was going to ask about religion, which I haven't done. But the mention of the Episcopal Church – were you, were you church people?

KR We were… My father was, definitely was not, and did not go to church. And my mother was, and was influenced by her mother – my grandmother – who was very religious. And this had an influence on the rest of the family and all the family did go

to church. But I would say that my mum, my mother probably kept her faith, and of the children I don't think any of us really could be called…

MB You didn't get caught up in that?

KR …fully involved in church matters.

MB When you came to the sixth form, it was clear that you were going to do science? Was that clear? You'd decided on a…

KR Yes, I…

MB …a career even, had you?

KR I think, I think I was quite lucky in that I felt that chemistry was a subject I wanted to follow. And even at sort of two years before the Highers I was interested in the biological aspect of chemistry. So it was biology and chemistry I was interested in. But you couldn't, I don't think you had the opportunity to do biology at that stage. So I concentrated on chemistry

MB Right. But how did the biology then come along, that side?

KR That didn't really emerge until I went to university, although I was doing background reading on that, on my own.

MB Right, it gripped you a bit.

KR Yes, yes.

MB I've got a feeling, at one time when we talked you said there might have been a pharmacy career, just a bit in mind. Was that, was that right at that stage?

KR Yes, I was interested in the effects that chemicals had on the body, you see, and that fascinated me, and I…

MB You had expectations of working in Boots, you said.

KR I mean I didn't really know much about the opportunities in medical research and I, living in a small town I thought a pharmacist might be the person developing the products that…

MB Who at school provided the real fuel for that scientific interest?

KR We had a man called Wiseman in the final year at school, in our sixth year at school. And in fact I achieved the university entrance by my fifth year at school. I was fairly young, seventeen, just about eighteen, and I decided to take another year before going to university, and I spent the sixth year at Peterhead Academy doing some more chemistry and advanced maths. And he, this man encouraged us to really do experiments on our own, just left us on our – there were about five of us, and we used to do crazy things like isolating iodine, I think, and algaenates from seaweed.

He had us collecting seaweed from the shore and drying it on the roof of the, of the building, which rather irritated the headmaster of the school!

MB Who wouldn't want the stink around the place!

KR But he did…

MB Did he get

KR No … I, for some reason I don't think we used most of it, we left most of it on the top of the wretched school! But he did encourage us to do things on our own, and I think that that was very good for university when you had to do practical classes on your own.

MB So you felt a bit towards research by the time you actually left? You'd enjoyed that. I also have an idea that you, you might have had some chemistry at home, from an early competition(?) that you'd collected bottles of chemicals and chemistry sets…

KR Yes. I don't know if it was my parents or some, some relative gave me a chemistry set when I was about – I couldn't have been more than about seven. But I got fascinated by this and…

MB That happened to me and it had a frightfully dangerous…

KR …little paraffin burner and these test-tubes in which you would heat things up – sulphur and things like that, and obnoxious smells…

MB And things would fly!

KR And things would fly!

MB I don't think it's allowed now.

KR It's … yes, I don't think, I can't remember them selling or providing safety glasses or anything like that with it, which is probably not allowed these days.

MB The decision to go to university in Aberdeen, that was pretty automatic for people who were in Peterhead. Was that, was that right? You went to your local university?

KR It was, Aberdeen is thirty-two miles from Peterhead, and it was, most of the people who went from Peterhead Academy to university would have, would go to Aberdeen. It was just the traditional thing to do. And I think that the other Scottish universities – for example Glasgow – would be full of people, the university would be full of people from Glasgow. Edinburgh and St Andrew's attracted more people, a lot of English students and overseas students. But Aberdeen was really eighty, at that time eighty/ninety per cent of people were from…

MB And in the early sixties…

KR …from Scotland and from the Isles.

MB …In the early sixties it was very strong in chemistry, I believe.

KR Yes, it had a…

MB I mean it really was a strong chemistry department, moving…

KR …it had a large chemistry department, and I was amazed that recently that it was essentially closed down. And it's just a sign of the times that…

MB Ken, you're virtually eighteen, and you're about to move to Aberdeen – we've got you to that stage. Let's do a quick analysis if I can, you've kind of become a fairly established kind of worker in your own right, you've developed confidences, you've become a Queen's Scout by this time, you've become a competent tennis player, winning local tournaments. I think we've talked about that before, haven't we, I know a bit about your tennis from our own encounters. And I'm just wondering were there any other aspects of life? I mean, girlfriends – had they formed by then? Or were you too serious about…

KR Nothing, nothing very serious! Flirtations at the tennis club, and things like that, but that was nothing…

MB What about things like theatre and cinema?

KR Cinema, yes I think that that really… I saw a lot of films in my youth because my godfather was a man called … John Bannerman Milne, and he was a self-made millionaire who was an entrepreneur who bought up cinema houses all round Scotland. And this was in the era when cinema was very popular in the late forties/fifties, and there were huge queues to see these films, and…

MB And you had complementaries to go every week?

KR I had complementary…

MB From this godfather?

KR …tickets from my associations.

MB And Bannerman Milne, this accounts for the…

KR That's my middle name – Kenneth Bannerman Milne Reid.

MB So you were really into celluloid in a big way.

KR I certainly, I probably went once a week, yes, to the cinema!

MB Let's move to that Aberdeen period. Was that a culture shock? Did you go into digs, first time away from home?

KR Yes, it was, because sharing digs with, I suppose it must have been fourteen or fifteen others in my first digs, these huge houses in Polmuir Road in Aberdeen, this landlady called Mrs Mutch who used to organise us all and try and get us all out before nine o'clock for the first lecture! And … I think we were all science students as well. And in some ways it was an enjoyable time, but it was a different, different from… I, living in Peterhead where I was literally fifty yards from the school and just walked across the road to the school, I had to fight my way through the Aberdeen rush hour traffic to try and get to these nine o'clock lectures.

MB Was there a separate science block at the university?

KR Aberdeen was divided into two areas: Marischal College and King's College. And we had lectures on, at about just over a mile apart, and we had lectures on both sites.

MB Well, you must have done some running!

KR So we had to go backwards and forwards between these two sites.

MB What was it like, chemistry though, in your first year?

KR I, the classes were rather huge – I supposes there was, as nowadays in most of the big universities, sort of a hundred and twenty… And some of the lecturers were very good and showmen, and really generated enthusiasm. Others were rather dull, I suppose it's just the same in a lot of universities – a lot depends on the personality of the lecturer.

MB What was the chemistry like though?

KR The…

MB Was it like inorganic at that stage?

KR I must admit I didn't enjoy the inorganic and physical chemistry, especially in the sort of second and third years after I'd decided to commit myself to biochemistry. The first year of course I dutifully did all the subjects as well as I could and…

MB They had a number of basic disciplines, didn't they? I mean that's, that's how it started at, in Scottish universities. Was that right?

KR In maths…

MB Kind of maths and…

KR There was a lot of flexibility, understand(?) we had a lot of flexibility in university courses at Scotland. You could do four, usually did at least four subjects in your first year, and you didn't necessarily have to do any of these subjects in the second year. And it would be usual to…

MB So you could have a look around?

KR The second year was the starting point for the, the degree.

MB The four-year course.

KR Four-year course, yes.

MB And was that first year a time when you had a chance to get some biology? Did you, did you opt for that?

KR Yes, I did zoology then, and that stood, well ensured that I, to me made my mind up that I wanted to go into the biological aspects of chemistry. And the chemistry course did have, the organic chemistry course did have some more biological aspects to it. And that confirmed in my mind that's the way I wanted to go.

MB And so you followed, eventually, biochemistry?

KR That's right. Yes, in the second, in the second year I took, I started a biochemistry degree, so…

MB And your degree ultimately was a biochemistry degree?

KR I did biochemistry and physiology in the second year, as well as chemistry. It, I was obliged to do four years chemistry.

MB Did the [in]organic, did the [in]organic stay all the time as well? Did you have to keep…?

KR No, after the second year…

MB You could drop it?

KR …the people doing biochemistry could drop out of inorganic chemistry and physical chemistry.

MB And they covered, from what you said there weren't any lecturers who particularly stood out, but there were some, there were some showmen?

KR This man called Moser[1], who used to do things like the iodine clock: which you'd had the colourless solution, which you would then get a stopwatch out and count down to the change of colour, and then the whole audience would applaud!

MB Great days! Do you think you came alive, from what you've said, when you got a chance to actually do hands-on research? That was a really great time, and that was the honours project towards the end of the course.

[1] Wolf Moser.

KR Yes, I think this was always a very important aspect of any chemistry or biochemistry degree. And I, I've seen this at Oxford University, that the students get really involved in the research topics that they're given. And this was the same in my case, at Aberdeen University – I spent a whole term and really got very motivated into doing this work.

MB Did you chose a supervisor or a project?

KR I, as far as I recall we were just given supervisors, and then the supervisor talked to you and we discussed the project. And the man that I, who acted as my supervisor, was a man called Patrick Grant. And he was working on carbohydrates that were isolated from fish. I mean it could have been from any animal, but he had a, he was going, he'd just been appointed director of the Fisheries Research Unit, and he was spending a lot of time setting up projects and organising the building. But, one of the projects he was interested in was the carbohydrate units on a polypeptide chain, and these are so-called glycosamino glycuronoglycans, which are sort of embedded in my memory because it was one of the first projects that I worked, worked on. And I was looking at the way these large carbohydrate units were linked to this polypeptide backbone and the serine residues.

MB Right, so you're looking at the serine residues.

KR And then I used some of the chemistry, chemical techniques to show that, prove that this linkage was involved in serine residue. And at the time this was quite innovative work, but unfortunately somebody else had done exactly the same thing and published it in the *Journal of Biological Chemistry*, and it was a bit…

MB While you were working on it?

KR Well it was just after I'd written up my little project, and the supervisor, we were writing a paper to write this up. And as in science, if something's interesting you'll probably find that somebody else is doing the same thing.

MB A taste of scientific disappointment.

KR So, yes, it was a slight, slight disappointment, yes…

MB But it was work that was really quite original?

KR …on the other hand, on the other hand I could see that it was work that was of some interest, scientific interest, and worthy of publication. So it illustrated to me that it had done something useful in that term.

MB Were you interested in glycans themselves? Did they, did they grip? Or was it just the techniques and the application of…

KR I was more interested in the protein aspects even then…

MB Right.

KR …and I must admit it's more recently I've got back to thinking about carbohydrates. But I think in the bulk of my career it's been protein chemistry rather than carbohydrates.

MB So I can talk about carbohydrates with you in your more recent interest later. Patrick Grant – did he, did he kind of provide an interesting model to follow? Did he become a person of great interest, quite quickly?

KR He was an unusual character, another chain smoker who used to – I remember when he used to give me a lift in the car, because I eventually did, did work with him. And he used to go between Marischal College and his Fisheries Research Unit in Torry, and he always had to have a cigarette in his hand or his mouth, and he used to juggle the steering wheel of the car while he lit his cigarette, and…

MB He was flamboyant?

KR Yes, he was an extrovert character…

MB A good lecturer?

KR He was, he was a good lecturer. He conveyed the ideas to the students very well.

MB But I get an impression that at that time he was busy and, in a way kind of left it to you, this project. And that probably had an influence.

KR I think that was helpful in a way. He was always willing to talk to me if I had results. And there was a postdoctoral worker in the lab who was very helpful – a woman called Thelma Fletcher who I've kept in touch with all these years. And she was extraordinarily helpful in showing me the procedures for analysing the carbohydrates and things like, things like this, and I think that's always important in a good…

MB In the lab in which you worked, that was…

KR …in a good lab, if the senior people…

MB In Marischal College?

KR That was in Marischal College.

MB Yes. And so you turned in this rather exciting project that you felt was good, and that I think they felt was good, and completed the degree course.

KR Yes I finished my honours degree there and Patrick Grant did have this studentship available, from the Medical Research Council, and he offered it to me. And at that time I'd really got interested in medicine, I knew I was, I was perhaps lucky, I knew I was going to, I wanted to do medical research and I felt that I should get a medical degree. And with hindsight I, I'm not sure, I was probably not correct – you don't need a medical degree, I don't think, to do medical research. But I got in, I

was given interest to medical school and I was going to start on the second year of a medical degree course when I was offered this MRC…

MB So you were going to go through medicine for a further four years?

KR …I was offered this studentship, and I had to decide at the sort of, sort of mid-summer I really had to make a decision and I decided to go for the studentship.

MB But you'd gone quite a long way down that road of deciding to do medicine?

KR Yes, I…

MB Getting finance sorted and various things.

KR …I, my father had… Since I'd done a first degree it would have been counted as doing another first degree, therefore I wouldn't have received a grant from the education authorities. My father said he would provide the funds but I felt that was unfair so I decided to take the studentship because essentially it was going to take me more directly to medical research.

MB Just staying at that particular point, Ken, we've got four years of Aberdeen, the kind of undergraduate years. Just to put on the map, I think the sport continued. I think you were a kind of leader of the tennis group at the university, and I should put that on the map. You were fairly lively, had a lively…

KR I, when I first went to Aberdeen my interests were … in the winter I played badminton and I represented the university at badminton and was treasurer … and held various offices in the club. And in the tennis I represented the university at tennis and was on, I was captain of the tennis team for several years – especially since I was a postgraduate…

MB Right.

KR …student there as well, so there was some continuity.

MB Anything else about Aberdeen we should have on the record before we move to kind of … postgraduate studies? Anything else? A fascinating town.

KR I think … that's, it's a very fascinating city to spend your university life in – it's two hundred thousand population so it's not a small…

MB Yes.

KR …city, it's quite lively. And there's a lot of things going on – a lot of opportunities to do things, and social life, and arts and…

MB So you joined in with all that and kind of grew up another, another step in that period.

KR …a lot of concerts, and theatres, visits possible.

MB Ken, at this particular moment I'm going to wind down – we'll take a quick coffee, and then we'll come back and take you to postgraduate research with Patrick Grant. At the moment we'll wind down.

KR Okay, fine.

MB Ken, you went on an MRC studentship to work with Patrick Grant in his new Fisheries Research Unit.

KR Yes, he was the director of this Fisheries Biochemical Research Unit, and so he was my main supervisor. And I also had a supervisor who was located at Marischal College – a man called John Sargent.

MB So he was the university supervisor?

KR Yes he, he was – I got one of the better lecturers at Marischal College.

MB And he was a biochemist too?

KR He was a biochemist. And the project involved study on the structure and the biosynthesis of insulin from the cod.[2]

MB Right.

KR And the project really stemmed from the fact that you can, in these fish you can look at the insulin biosynthesis very easily by isolating the gland, the so-called islet gland which is located on the gallbladder of the, of the cod fish. You can just snip that off and put it into a buffer with a, some radioactivity to tag the biosynthetic properties. And then I, you can isolate the protein and look at the, how it's being formed and how it's being processed.

MB Who chose that project, was this the one choice?

KR That was one of Patrick's – his idea was to look at the… It wasn't really known at that time whether insulin was synthesised as one long chain or whether it was synthesised as two chains and then held together by disulphide bonds. And this was, there were various laboratories round the world looking at this and…

MB The insulin was a bit in focus at that time?

KR Yes, there was a lot of interest in it, some groups were crystallising it and trying to do the three-dimensional structure of it. So it was a, quite a good project for a young PhD to be doing, I think. And one of my first jobs as it were in the lab was… This was done at Marischal College because the buildings weren't quite finished out at Torry where the, the Fisheries Biochemical Research Unit was being put up.

[2] *Insulin of cod: Primary structure and biosynthesis*.

MB Was that on the kind of harbour-side?

KR That was in fact overlooking the harbour – you could see well out to sea, and over…

MB Terrifically ocean…

KR And one of my first jobs at Marischal College was taking commercial insulin and running it down a column to separate out, to see how pure it [was], and use that as a marker, and I noticed…

MB You went up, you went out to the pharmacy and brought some back?

KR I, no you could, commercial insulin was produced in large quantities because it was a very important drug, but… I was able to chromatograph that, and I found a small peak just before the real insulin peak. And this turned, I asked my supervisor what this was, and he said 'Oh, it's probably a contaminant.' It turned out to be a precursor of insulin, which I think … I'll tell you a bit more about the project later. But it was, in fact it would have provided the proof that insulin is synthesised as one chain. So I had in my hands the possibility…

MB A possible discovery…

KR …of working this out in the first month! But I put it aside. But, it was in the days before amino acid sequencing and amino acid analysis was in its infancy. So it was very difficult to categorise these fragments and…

MB And I take it you were at the stage of kind of hydrolysing kind of protein chains.

KR A lot, a lot of my, when I did move out to the new institute out at Torry – the Fisheries Biochemical Research Institute – I spent a lot of time doing amino acid analysis, that's breaking down the insulin, cod insulin into its fragments, and then you…

MB Trying to piece out the sequence?

KR You can piece out the sequence from it. Sanger[3] of course had done this for bovine insulin in the fifties, and that was the first protein to be sequenced, the bovine insulin. So I was really following some of the steps that Sanger used, and also using recent advances in sequencing to do it much faster. I mean, now the work that I took sort of a year and a half to do for the cod insulin could probably be done in a few days in a modern laboratory.

MB Did you have to go and collect these glands? I mean, what actually happened?

[3] Frederick Sanger, won the Nobel Prize for chemistry in 1958 for his work on the structure of insulin.

KR That was probably, the two worst weeks of my life were spent on a research trawler in the North Sea…

MB Well you did, just didn't go down and get the fish from the dock…

KR Initially I collected a large number of these so-called islet glands myself, I dissected them up and freshly caught cod on this research trawler. And I just got several thousand of these glands, and froze them away. But I was seasick for the complete two weeks. And I don't know if you've ever been seasick, but you reach a stage where you've got nothing in your stomach except the bile juice. And you, and of course as I mentioned this gland that I was working on is situated on the gall bladder of the cod, which is, of course when you puncture that bit it's got bile juice coming out of it. So it was a really…

MB You were violently ill(?)

KR …bad two weeks for me! But I got the material that I needed to do the structural work. And thankfully all the biosynthetic work I could do with small numbers of cod which were caught locally, and we had fish tanks in the institute.

MB Ken, at this stage we might bring in your future wife, Margery, who I think provided a lot of support going down and collecting, collecting fish materials.

KR Yes, we used to collect these fish, probably at eight or nine o'clock at night, because these small boats used to go out… A very hard life – they'd go out quite early in the morning but they wouldn't come back till about eight o'clock or nine o'clock at night. And they would also, they would collect some of these fish guts as it were, and I'd get the, more islet glands from that because I always, we always needed a lot of this insulin for crystallography studies and for functional studies. And, but they also brought back live fish in large bins, which Margery and I transported up to the Fisheries Biochemical Research Unit and put into tanks in the basement of the building. And, I was always impressed that these relatively deep-water fish survived the experience, and they could live for months in this environment. And we used them for experimental purposes, obviously…

MB And you'd do this, and Margery…

KR …biosynthesis and…

MB …used to help dissect out the glands, night after night on occasion.

KR Yes.

MB A labour of love you described it as! And this became a kind of lifelong relationship.

KR Yes, I think we met in the first year of my…

MB That was about '61/'62?

KR …PhD. Yes, sort of '61…

MB And that… Let's just take a couple of those issues. You were obviously trying to break up insulin, looking at its characteristic amino acid kind of sequences. But you talk about the crystallographic side, getting crystals – was that an easy side, did you get into that side as well?

KR Mm, insulin is one of these proteins which crystallises very easily in fact, so as, as a young PhD student I was able to produce crystals in a few weeks with insulin. But they were, I in fact came down to Oxford and met Dorothy Hodgkin and her group, and gave them some of my cod insulin crystals. I don't think they were very impressed! Because you really, you needed really large crystals for the crystallography studies, and they…

MB But you got to meet the team down here – Dorothy's team?

KR Yes, I go to meet them. And the, they made larger crystals and they were, they were looking at the 3-D structures of various species of things.

MB While we're dissecting into that crystallography side, I wasn't clear whether crystallography had got very far in the Aberdeen kind of arena.

KR Mm, there was nobody in, in Aberdeen doing…

MB And so you were doing crystallography, going outside for help with, with crystals?

KR Yes, and it wasn't a major part of my project. It was a sort of side issue.

MB And day in day out you'd looked at amino acid sequences?

KR Yes, I used to spend…

MB You never went home at times?

KR …I used to spend weekends sitting, feeding this amino acid analyser. It took about a five to six hour run, say, and I was quite interested in the results, so I'd watch some of the results to come off! And then I'd…

MB Like waiting for crystals to form?

KR …I'd go in, and do something and then come back to the institute, because I knew that the machine, if you, it, there was no automatic loading of the machine, you had to manually load it. And I'd put it on for the next five or six hour run and…

MB Radioactive material you were using… I got an impression that you were still left, with Grant, largely on your own. I just wondered where all the skills came from – whether you built them in yourself or whether you had enough time with Grant to develop techniques?

KR I, again you could argue that it would be better if he had been more, supervising me more closely, but I think it was very good that he left me on my own to make mistakes and learn by mistakes, and…

MB I'm taking it that this wasn't an intention of his but that the pressure of setting up a new institute actually prevented him from being really involved.

KR Yes, it was literally the first sort of six to nine months of the, of the institute, and he had to recruit new staff for all our laboratories and set up projects for them and discuss matters with them. So, in fact I was given a whole laboratory to myself – it's the most space I've ever had in my working life as a scientist.

MB You wanted to be a research scientist. Was it as satisfying as you'd believed? I mean, you really did get hooked.

KR I got enormous satisfaction, as you might imagine, collecting the raw material yourself, processing it, and then analysing it in great detail. And it was very satisfying. And also getting evidence from the biosynthetic studies for this so-called proinsulin, the precursor for the single chain form of insulin, which is then, is converted – there's a bit chopped out, the so-called connecting peptide which connects the A and B chains of insulin. And we got rather nice evidence for the processing that takes place. And there again it was a very intensive period in, in insulin research, and there were people in Chicago doing very similar studies using so-called insulinoma – a cell that produces human insulin…

MB Was it started in Chicago?

KR …and in, this was a man called Donald Steiner in Chicago. And, in fact he got interested in our work and came and visited us, I think just to vet us, to see what we were doing. But I think he, he published sort of six months before us – again we seemed to be sort of pipped at the post as it were in terms of…[4]

MB About the kind of, kind of proinsulin.

KR …the proinsulin story.

MB Proinsulin, yes. So you were beaten, but you might have had that earlier if that first column kind of separation…

KR Yes, I remarked about the fact that this apparent contaminant in the insulin preparation was in fact proinsulin, and…

MB You, but sooner or later you published on certain points about…

KR Oh yes, we published several papers on…[5]

[4] DF Steiner, D Cunningham, L Spigelman, B Aten, 'Insulin biosynthesis: evidence for a precursor', *Science*, August 11 1967, 157:789, 697-700.

[5] These included: PT Grant, KB Reid, 'Isolation of a partial amino acid sequence of insulin from the islet tissue of cod (Gadus callarias), *Biochemical Journal*, January 1968, 106:2, 531-41. PT Grant, KB

MB And you write up, within two years – it was about two years?

KR No, it took three, it took three years, yes.

MB It did take three years? It did go the distance. You eventually wrote up about the biosynthesis, and about the structure of cod insulin.

KR And … I took, I took it a bit further – I was appointed, Patrick Grant wanted me to stay on in the unit and offered me a scientific officer position.

MB So you became a civil servant?

KR It was funded by the civil services, and I was given a tenured civil service position!

MB So you got a job, yes.

KR That's immediately after finishing my PhD. But I hadn't really thought of staying long-term there, and I'd written to Cambridge, to Sanger, and also to Arnstein[6] in London, and…

MB Ken, I'm just going to hold you at that particular point though, because I'm just going to keep to the PhD being handed in, and being marked. Because you had a rather, a rather interesting examination, that I, that I think we should discuss.

KR Well, coming from the north-east of Scotland I was quite a quiet and reserved, probably still am fairly quiet and reserved person. So somebody examining me had to pull things out of me in a way. And examinations in Scotland involved the two supervisors – so Patrick Grant was there and John Sargent was there. They're, they're both rather extrovert and loquacious, but they're not supposed, allowed to say anything because they're supervisors of the, of the student. Then, the professor is also there – he was a man called Kermack who was, he was blind. And so he usually chipped in but of course other people had to lead, helped lead the conversation usually. And my examiner was Rodney Porter, and he was … rather abrupt and to the point when questioning! And apparently, well Patrick Grant could hardly contain himself because the, I think the viva went rather quickly in terms of the very short…

MB Few exchanges?

KR …short questions and answer!

MB And … shortest on record is it? One of the, of the shortest examinations ever?

KR But he, Rod Porter was very pleased with the thesis because it was his type of work. He was interested in protein analysis and sequencing, structure function relationships. And in fact I had probably more conversation with him after the viva

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Reid, 'Biosynthesis of an insulin precursor by islet tissue of cod,' *Biochemical Journal*, November 1968, 110: 2, 281-88.

[6] Henry Arnstein.

than in the viva! I think he probably found it inhibiting as well to have the two supervisors there and the, and the blind professor, Prof Kermack…

MB Kermack, yes, he was…

KR He was blinded…

MB …he was very effective despite the blindness.

KR …in an accident in Edinburgh, I think, when he was a postdoctoral worker. But he was the first professor of biochemistry at Aberdeen, and he was a…

MB Coped brilliantly, did he?

KR …very effective lecturer – he used to give lectures on enzyme kinetics without… He had some Braille notes but he remembered everything that was on, was on the slides and could quote the whole, all the equations. And I think it was probably a bit of showmanship – to impress the students! But he also showed this facility, he would go to lectures and seminars and then he'd pop up afterwards and ask questions about slide number five when the speaker said such and such. And he was really a, quite an impressive man.

MB Ken, that thesis – talking about impressive, that thesis was impressive. It didn't, it did consolidate a lot about fish insulin.

KR It grew as it, I think it was useful to look at another species of insulin because there is conservation of insulin structure overall, but the residues change when you look, compare a human with fish. And it's surprising that fish insulin can be used effectively in humans. And the Japanese showed this during the war when they had problems in getting the conventional animal insulins – the bovine insulin or the pig insulin.

MB You talk about when that project was through, it was very satisfying. You put that insulin to one side a bit in your mind and thought 'I want to go on to human … biochemistry, not animal biochemistry.' And you were suggesting that though you worked for a time as a, as a civil servant in Grant's unit, you started to look out fairly quickly.

KR Yes, I made applications to Sanger in Cambridge, Arnstein in London and Porter in Oxford…

MB We're talking '68/'69 now?

KR Yes.

MB The thesis was finished in '68.

KR '68, '68, yes. And I wrote applications for Fellowships to study, and Sanger said he might have something available in about a year to two years time. But being young and impatient I said 'Well, I should hop all(?) up to London and Oxford and

openings.' And I wrote Fellowship applications to go to London and Oxford. And one of these came through – an ICI Fellowship application which, I'd visited Oxford and met several people and talked to them about immunoglobulin structure and function, human immunoglobulin structure and function. I found that a fascinating area and that's what I put forward in this ICI Fellowship, which Porter supported. And perhaps his name had helped the Fellowship go through – I think there's no harm in … putting down a good lab in your Fellowship application. And if he was willing to take me I think that that probably helped as well. And so I got the opportunity to go there. I gave up my position at Aberdeen, which, with hindsight, it was a bit strange to give up a tenured position to go to a two year, and take a cut in salary to take a two year postdoctoral position in Oxford.

MB I'm just thinking whether the insulin work had gone on in the two years, whether you kept things ticking over in that particular direction, or was it an enormous move?

KR It was one, it was an extra year I spent doing on the biosynthesis of insulin, and that produced one more paper.[7]

MB '69 arrives, and you make that move, from Aberdeen to work in Oxford, with Rodney Porter in the biochemistry department, where he was the Whitley…

KR Yes, he was, he was the Whitley professor of biochemistry so he was overall, in overall charge of the biochemistry department.

MB Yes. But before coming South, you actually married Margery and moved down as a, as a married couple.

KR Yes, we spent part of our honeymoon looking for accommodation in Oxford! Which is a, is quite a…

MB You were saying about that marriage, it was curious in the sense that people - people in the institute, at the university - seemed to feel that was difficult, a technician actually marrying a…

KR They … were uncomfortable about scientific staff mixing with technical staff. A strange situation!

MB That was a kind of thing of that time – I can't think of it now, but that was a thing of the time.

KR It was sort of a them and us situation, I think.

MB But, but that marriage took place, and soon afterwards you came and found accommodation in Oxford, in north Oxford.

KR Yes, and Margery got a position as a, a technical position in the microbiology department, which was part of biochemistry, and...

[7] This might be NS Track, KB Reid, 'Structural comparison of mammalian and piscine insulins', *Hormone and Metabolic Research*, November 1969, 1:6, 255-57.

MB Right. But you didn't think you'd stay in Oxford, you didn't think…

KR We, we envisaged staying two years. And when we first came we, it was October, and obviously…

MB You didn't like it?

KR We … we thought it was an awful place, because we found it humid and oppressive. Of course we'd come from the north-east of Scotland where there were sort of bracing winds and rain every day of our lives! And to go to somewhere almost the centre of England was probably a big change to our … constitutions as it were. But now we've become rather soft and find it hard work when we go back to Scotland! We find it rather cold and dismal!

MB Ken, I just want to tease out, dissect out the strands in the development of your research in Oxford. You'd come down and spent some time with Rod Porter before making the decision, and had seen what was going on in the lab. And you'd talked to someone who was going to have a big influence on the direction.

KR Yes I, I met a man called 'Newt' - Newton Hyslop – 'Newt' as he was called in the, in the lab. He was a visiting American worker who had a sabbatical year essentially, and he was interested in what was called the compliment, the serum complement system. It's a whole battery of proteins that are brought into motion, or one pathway of them brought into motion by antibodies recognising something as foreign, and triggering off this system. And he was interested in the way that complement was activated by antibody-antigen aggregates. And that was going to be my first job – that was my first job, was to make stable forms of hapten antibody aggregates, which activated complement. And the…

MB That was his interest, and you took that on board. But you saw a bit further than that I think, Ken.

KR Well, I was able to make these stable forms of the, of the complexes, but it was trickier to… The prof, Rodney Porter, was interested in the physical aspects of the antibody-antigen complex, and he wanted to do more physical studies on the, on the complexes. But I felt that that was going to be, require new techniques which we didn't have ready access to. And, I felt that there was a lot to be learnt about the other arm – the complement activation arm of the antibody and the complement proteins themselves, and that that…

MB There was a lot of protein chemist in you – that was where you were coming from. That would be right?

KR And my background doing … amino acid sequencing and protein analysis and structure-function relationships, and the insulin work and proinsulin work, I suppose influenced me in some respects. And also at Aberdeen I, just as a side issue I'd taken an interest in collagen structure and function, just because I found it interesting. And this paid off because one of the complement proteins in fact had collagen-like structure, and I was able to very quickly establish an overall model for one of the

complement proteins. And given that I was, had the background in doing protein analysis and protein sequencing and had this knowledge on the collagen structure…

MB So within the first year of your, that came out? Which protein was that?

KR It was protein called C1q, so I did some functional work on the activation of the complement system, which involved antibodies called, the Fab portion of the antibody which binds the antigen. And the other portion – the F, so-called Fc portion of the antibody, the tail of the antibody interacts with this protein called C1q, which is the first protein in the complement system, and triggers off the…

MB The whole sequence of events…

KR …the cascade of the complement system, and…

MB …that result in the efficient attack of pathogens.

KR Pathogens, yes.

MB Ken, I'm going to just hold you at that point, because that's getting us into a complex story of the complement system. I want to ask you, because we've arrived in Oxford, we've had this kind of weather shock, this climatic shock, was there a culture shock in going into Porter's lab? Was it, was it different to anything you'd had before? What was Porter like? I'm asking a lot of questions.

KR … Rod Porter was a very easy person to interact with. For example, when I came down for my interview, I was impressed… I was told to go to the fourth floor and find the professor, he was sitting at a spectrophotometer reading the optical density of tubes, and with his shirt-sleeves rolled up, and was really doing very down-to-earth benchwork. And, this was the way he approached things all the time I was there. He would get into the lab and talk to people and try and get to grips with what was happening on the bench. And he was very encouraging – he would talk through experiments with you and try and push forward new ideas, or try and solve problems. And … and I suppose a good illustration of how he kept you going was, if you… He would encourage you if things were going badly, but if things went exceptionally well, and you felt you'd finished some piece of work, he'd say 'That's great! What are you going to do next?' That was sort of forgotten, and it was on to the next thing.

MB A motivator.

KR So he kept the, he always kept the momentum going.

MB And you had a lot of distinguished visitors coming into that department.

KR And I think that was a very healthy thing. We had – and it's something which has been retained in the unit all through his time and more recently – we have a core staff in this Medical Research Council unit (he was professor of biochemistry but he had a Medical Research Council unit), this core staff of about four scientists and some, and five or six technical staff who are there all the time. But the rest of the unit would change over in sort of on to three-year intervals. There would be students

coming in for three years, and visiting workers or other scientists coming for sort of one year or two years at the, at the most, bringing new ideas. And this, this I think is a very healthy environment.

MB So it was highly stimulating, and you got moving. And we could now probably take in the idea of the complement system, which is incredibly difficult for anybody outside. And so we'll probably … take a look at it, now if I could, through your eyes. Complement I've always thought of as a series of proteins. You've talked about them – soluble proteins in the, in the serum of the blood – that are able to work with antibodies or independently to form kind of complexes of protein that will damage the membranes of pathogens. Am I, am I right in that? But, it involves an enormous amount of safeguards, because it could so easily turn on self, and ones' own cells.

KR Yes, the whole system involves at least thirty proteins and cell surface [molecules] – these are soluble proteins and cell surface molecules – and some of them are involved in the activation scheme as you mentioned, and in a cascade fashion. But of course, cascades are very dangerous if they are allowed to continually activate, and they have to come under the control of a variety, at a variety of positions. And the system can be simplified really in thinking of it having two arms – one an antibody-driven arm, and so the antibody has to recognise a foreign bacterium or virus as being foreign, as being required to be eliminated. And once the antibody has fulfilled its recognition role, it calls into play the so-called 'classical pathway' of the complement system, which involves this protein C1q which…

MB That's the first…

KR …I did a lot of work on.

MB …compound involved in the sequence of events in the cascade.

KR In the so-called classical pathway, yes.

MB Take me through that. And this is, by the way I'm picking up a book that you wrote with Alex Law.[8] Just take me through that. Once an antibody has actually focussed or groups of antibodies have focussed on a, on an invading cell, then they are an attraction site for the classical compensation of complement proteins.

KR It's remarkable that you have one antibody Ig, the so-called IgM class antibody, on the surface of the cell recognise something foreign on the surface of the cell. This can cause a, great amp- … once the complement system has been activated, there's a great amplification event takes place. So you can have up to a thousand of the so-called C3 molecules… The most abundant of the complement proteins is called component C3, and it's a milligram per ml in the bloodstream. And up to a thousand of these can be activated at the site of one antibody molecule recognising something as foreign. So there's a huge, you can see there's been an enormous amplification of the system in the early phases. And this, the fragments of C3, some of them are involved in drawing inflammatory cells towards the site where the foreign

[8] SKA Law and KB Reid, *Complement*, Oxford; Washington DC: IRL Press, 1988.

micro-organism might be located, or the lesion might be located. And there are so-called terminal components in the complement system, which can actually form a plug which forms a hole in the… The target can, the target can be a foreign cell or it can be a bacterium or a virus, and the complement system…

MB It's like a grommet, goes through, is formed virtually through the wall?

KR Yes.

MB And it's leakage of the materials out that brings about the end of the…

KR Yes, yes.

MB …of the microbe. Ken, I'm going to take just one look at that myself to make sure I've got it clear. Could I do that?

KR Sure.

MB Antibody recognises, okay, complement protein C1 interacts with that basic link, that antibody on the wall of the, of the pathogen. A reaction prompted by that link of C1 and the antibody releases some chemical factor?

KR Well, it activates an enzyme from its pro-enzyme state to its activated state, and so this is how you…

MB It switches on…

KR …promote this cascade reaction.

MB Right, C3 is affected?

KR Yes.

MB And then C3 seeds in elsewhere locally, because it's very local.

KR Yes, unless…

MB From the pictures you've shown me…

KR …unless it reacts very quickly at the site of activation it, it is hydrolysed by water and becomes inactive, so that…

MB That's one of the safeguards, is it?

KR This is one of the safeguards in the reaction, yes.

MB So highly local, very quick. So the action of antibody complement reaction very quickly spreads C3s that are activated all over the adjacent membrane?

KR Yes, you have a bacterium with some antibody on the surface, but then it'll very quickly become coated with fragments of C3, which signal that this thing is foreign and has to be lysed and removed.

MB Incredible multiplication though, because you can get so many C3 fragments, you're suggesting a thousand-fold. I think there's a picture in this book, you… Can I, can I…

KR Yes, sure.

MB …go through it? You've loaned me this, I've been thumbing through pictures and I'm fascinated. [Dr Blythe shows a picture from the book.] That, that's your C1, is it?

KR That's a C1q molecule.

MB That's the C1, comes in…

KR …the heads which recognise the antibody Fc regions.

MB Right. Do you have a colour picture of those anywhere? Did you have a colour picture anywhere?

KR Great, yes, ah-ha.

MB We could, we could delve into that while I'm… That's the C1 linking with the antibody. I'm going to try to get that on camera two.

KR This is the C1q.

MB I'll put it that way round and then it will look … common…

KR That's the antibody in purple, and the C1q heads binding to…

MB A little bunch of tulips, all these heads binding in tightly to antibodies that have formed on the wall. And it's from somewhere here that you release the enzyme effect on the C3s.

KR Yes, the enzyme… There are two enzymes called C1r and C1s which sit on the collagen-like stalks...

MB On that kind of stalk, yes.

KR …these stalks of the C1q molecule.

MB So this is collagen-ish?

KR Yes.

MB Ah. And we finish up … let me, this is getting very, sorry, I'm getting very excited by this, I'm actually beginning to move into it. [Dr Blythe leafs through the book] There we are, we actually finish up with…

KR These are all(?), this is a surface of a red blood cell which has got antibodies stuck on it, and then complement has been added. And these lesions – I don't know if you, if you can see on the camera – but they are very discrete, and are all of the same size, and these are the so-called terminal components of complement C…

MB They're moving in.

KR complement C5 to C9, which form this…

MB That's our story though, isn't it?

KR …funnel … which…

MB That's part of it, that's just a…

KR …penetrates the membrane. And this is…

MB The surgical half(?) though of this particular kind of invasive grommet.

KR And this is work which was emerging in other laboratories. We concentrated really on the initial phases of the classical pathway.

MB And essentially you became an international expert on C1.

KR Yes, our strong point was protein chemistry. And as you, as I mentioned, there's up to thirty of these proteins in the bloodstream and on cell surfaces which had to be characterised. And in the late sixties/early seventies the procedures for looking at proteins were just becoming available for doing this detailed characterisation.

MB We should probably just take a thought about the state of the history of complement there is at that stage. Ken, I think there'd been some early reference to this kind of thing in the 1890s, and there's been further work in the 1920s. But it, it hadn't really taken off till protein studies got underway, am I right, that really got underway in the fifties and sixties?

KR Yes, there's … I think the early sixties were probably the most fruitful period in the, in the complement work. This man called Hans J Müller-Eberhard, he spent most of his research career on complement at the Scripps Clinic in California. And really due largely to his team the protein chemistry aspects of sort of isolating these various complement factors got underway, and he made a great contribution to the field. I mean, there were other American labs who also made contributions, but that's the name, the name that springs readily to mind. And he characterised probably about twelve or fifteen of these proteins, and worked out the reaction, was involved in working out the reaction sequence. So he, his laboratory and one or two other laboratories in the States had set the scene for … a lot of work to be done on the protein chemistry and sequencing.

MB So you were really on, in on the second wave in a way.

KR Yes.

MB But there was still plenty to do.

KR Yes.

MB We've talked about this classical pathway – that's only just one part of the story.

KR Yes, there is a pathway called the alternative pathway in which you can jump right into the C3 stage almost immediately. The organism is recognised as foreign really by a type of innate immune mechanism. There are structures on the surface of certain bacteria, which are recognised as being foreign by the complement protein … complex involving C3. What happens is the organism lets this complex be set up on the surface. Normally cells will clear this alternative pathway complex very quickly, but the alternative pathway is activated by certain bacteria, and their…

MB So, a fundamental kind of carbohydrates, or things typical of the outer surfaces of bacteria…

KR Act as a focus for the activation of the alternative…

MB …but not found in higher organisms…

KR Yes.

MB …would be, would be a basis for that recognition.

KR Yes.

MB And complement will form, once you get to the C3 stage it's activated. It will start to marshal the ingredients on the surface of that…

KR That's correct, it uses the later portions of the complement system, so you get to these plugs which are formed in the cell, cell wall – the C, the later components, C5 to C9.

MB You see now what you call MAC, the…

KR MAC – membrane attack...

MB …membrane attack complex.

KR Yes. And this is one area which this, the USA were very strong in – the Müller-Eberhard's laboratory and Manfred Mayer's laboratory.

MB Just thinking phylogenetically, Ken, I mean, just thinking of the origin of immune systems. I mean, it seems that this alternative pathway for complement was … did it predate antibodies?

KR It's thought to be phylogenetically older than the so-called classical pathway.

MB It's still fundamental. It takes a far earlier and easier signal of foreignness than the antibody system allows. And so that goes into action pretty directly. It doesn't have to wait four or five days for antibodies.

KR Yes, the, you've sort of hit on the crucial difference between the two pathways. In the classical pathway you need this adapter molecule, the antibody molecule. But of course to mount an antibody response is going to take you certainly days, maybe weeks.

MB So what's the advantage of the antibody? I mean, why was this so selected for…

KR Well, micro-organisms obviously can change their surface, and the antibody, the immune system can adapt to that so that you can get antibodies formed in new structures brought up by new micro-organisms.

MB Yes, so the antibodies provide the adaptive elements, but the complement system provides the natural pay loads(?).

KR Yes, it's the so-called, the effector system. And it is always there to be brought into play.

MB Ken, I think we've all got into that – that's been very exciting. Just take us though, you were getting into this in the, in the kind of early seventies, and a lot of this was not quite clear. You've had to clear a lot of the structural and the… I mean, you were talking about parts breaking away from complement units and bringing in macrophages. So, not only does it provide an immediate attack on the cell by the kind of grommets we've mentioned, but it has a whole range of calling-up devices.

KR Yes, there are fragments from the molecule, the protein C3, a small fragment of 77 amino acids comes off that. And there's a fragment comes off C4 and C5, and two of the other complement components, and they're also involved in, they have inflammatory properties.

MB Yes. That could be dangerous.

KR And this is why there have to be these many control proteins. And a lot of work we did in the unit was on the control proteins, the so-called C4-binding protein, just binds in, binds the C4. And there's another couple of proteins – one called factor H and an enzyme called factor I – which are involved in the damping down of the activity of C3. They essentially split C3, and block it's activity.

MB Ken, in those early seventies you wrote a number of papers, you published in '72, '74, '76, with Porter…

KR Yes, that's right, yes.

MB …some of them, although he was reluctant I think on occasions, which shows something of his generosity.

KR The first few papers I published with my name, he said since I was a young postdoc it was important that I published with only my own name on the paper.[9] Then I had this model essentially built for the C1q molecule and I felt it really was something that had emerged from my being able to work in the unit. And I said that really he should be on this paper, and he agreed…[10]

MB That was the (?) paper?

KR …initially he…

MB Yes.

KR And that is the, probably the most important paper of that … time of the, my time in the unit in the seventies…

MB Yes. Can we just consolidate that view that we have of those early seventies? We've started to talk about you getting involved in complement and all the people around and the kind of interests that there were. But for you, your head was down looking at C1 effectively in that period. Were there any other distractions?

KR Well, of course I had three young children!

MB Ah! Yes, I wasn't meaning… Tell me about that.

KR Well, I ended up with three children under five, which took Margery out of the lab, and…

MB Your life changed dramatically.

KR But I was, I was a bit obsessive with my work, I suppose. So life revolved around three young children and then long … well, the rest of the time was spent in the lab!

MB And you haven't mentioned the decision to stay in Oxford. Everything's changed – you were going to go away one or two, in one or two years, there was no thought of a permanent job, I mean settled in Oxford. But it happened.

[9] E.g. KB Reid, 'Complement fixation by the F(ab')2-fragment of pepsin-treated rabbit antibody', *Immunology*, May 1971, 20:5, 649-58.
[10] KB Reid, DM Lowe, RR Porter, 'Isolation and characterisation of C1q, a subcomponent of the first component of complement, from human and rabbit sera', *Biochemical Journal*, December 1972, 130:3, 249-63.

KR It was, I was beginning to think of moving from Oxford when Porter offered me, Rod Porter offered me a position in70, well '71…

MB In his MRC Unit?

KR …In his MRC Unit, before my ICI Fellowship finished.

MB So you became a civil servant again, sort of?

KR Yes, I think…

MB Scientific officer.

KR It was a scientific officer position.

MB And you'd been on this ICI Fellowship, yes. So, very quickly, Porter decided that you were going to be built into that, to that unit – that is important to put on record I think.

KR Yes, he had made the decision I think a bit, a bit earlier than that, yes.

MB The C1 work occupies those years. By the time we get though to the '76 paper,[11] things were beginning to change a bit in the field. Protein structure had been okay for now, but I think DNA work began, recombinant DNA work began to take a new hold on the laboratory.

KR Although it seems sort of matter of fact now to clone the genes and the cDNAs [complementary DNA] for these things which encode for the proteins in the body, it was a major thing to clone cDNA that encoded for any human protein at that time. And we were very lucky in having a … this is, sort of illustrates the approach of the MRC unit in bringing in visitor from outside. A man called Mike Carroll, who came from Texas – he'd worked with Don Capra's group in Texas – and he was, he hadn't any recombinant DNA work. But he came to Oxford and went into pathology where George Brownlee … who'd come from Cambridge… And he brought over recombinant DNA methods with him, and Mike Carroll learnt the methods from Brownlee's group, and brought them over to our group…

MB To your unit.

KR …and that, I think that was very important. And I think that's where Rod Porter saw that the way things were going, and how the unit should move. And myself and others in the unit quickly became involved in recombinant DNA work. And we were, I think I can safely say that we were one of the more successful labs in the complement field. We were cloning and expressing complement components and researched those. And I think it's acknowledged that we did…

MB You were pioneering it in a way, yes.

[11] KB Reid, RR Porter, 'Subunit composition and structure of subcomponent C1q of the first component of human complement', *Biochemical Journal*, April 1 1976, 155:1, 19-23.

KR …contribute, we did contribute…

MB You were picking all complement protein genes, were you? Is that what you were trying to do, kind of…

KR Oh, in my own laboratory we cloned the three chains for C1, this is the so-called C1q molecule, the A, B and C chains – it's quite a complicated molecule, so it had to have three chains had to be cloned separately. And we cloned some of the control proteins – one called properdin, which is one of the positive regulators in the pathway, and another C4 binding protein. Other people in the lab were working on the C4, and on the factor H and the factor I and the C2. So we covered a lot of the aspects of the early activation scheme of complement and the control of complement.

MB Ken, I'm reading into this that you were, you were reading the structure now from the DNA sequence side, the triplet side, rather than bothering…

KR Yes we were…

MB …in any way to look at peptides.

KR In those early days, we were, we were told and we were getting the feeling that perhaps protein chemistry was on the way out. But, I think we were quite right, and in fact we put more effort into protein chemistry, which was the correct approach, because once you'd cloned the material and got some sequence that was just the starting point, because then you wanted to usually express the whole molecule and bacteria or yeast, or some mammalian system. And if you look at the function of the molecule by perhaps mutating one residue or looking at a fragment of the, of the molecule...

MB So you held tight to that protein synthesis skill?

KR Ah-ha. And we increased our expertise in, in protein sequencing and analysis, and fractionation.

MB Did you move at all, now you were in Oxford, towards the x-ray crystallography side as well?

KR We interacted probably more with people doing NMR [nuclear magnetic resonance] studies, so we had fragments of proteins available. And people in the unit had been able to produce fragments of these proteins of up to twenty – you have to keep up to under twenty thousand molecular weight if you want to use NMR techniques to get three-dimensional structure.

MB Right.

KR But, Bob Sim who works in the unit has had some very good collaborations with Iain Campbell, who was working in the biochemistry department and had been very successful in getting three-dimensional structures for some of the complement modules.

MB Where was that NMR work in Oxford at that stage? Was Rex Richards still involved?

KR He was in, obviously involved in setting up the NMR facility. We didn't interact with Rex Richards himself – it was all, it's always been with Iain Campbell or…

MB Right. And where were they based, the NMR people?

KR The, it, first it was the basement of biochemistry, but a new facility was built in, under the Rex Richards building, in the basement.

MB Keeping us back from the eighties for a while – that's a luxury period to look into in some detail… But all that was taking place, and you've mentioned Sim, who was I think one of your first research students.

KR Yes, Bob's joined, he was my second student, he…

MB When did, when did you first have research students? Because you've had a chain of them since.

KR Ah, '71 Diane Lowe joined me – she's now Diane Scott and still working in science in the Hammersmith Hospital.

MB So you started to supervise very early.

KR Yes. And she did work on C1q, on rabbit C1q – we decided to look at another species and, as well as human C1q, and she did work on C1q and the C1 complex, the r and s. And then Bob Sim joined me and worked on the enzymes – the so-called C1r and C1s which sit on the collagen…

MB (inaudible)

KR …stalks of the C1q. He did some excellent work on the r and s enzymes, and also one of the control proteins – a thing called C1-inhibitor which actually latches on to the r and s and forms a covalent bond with them and pulls them off the, off the C1q molecule. And that gives you this rather dramatic way in which the, that activation complex was controlled – the enzyme is just stripped off the complex by the inhibitor.

MB And so that was, that was Bob Sim, working on that. Ken, we've got you well into the seventies now. I'm going to take a break in a moment, but I just wanted to finally consolidate – you've got research students coming through, you're supervising very responsible work. And the whole of the C1, by '76 is structured, a lot of detail provided, and you've begun to look at a whole range in the second half of the seventies of recombinant DNA technology. So you're ready for almost a new era, and when we come back for our second interview, it's that new era that I want to move into and travel through into the eighties. But for now, let's just take a break.

KR Thank you.