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Professor Sir Roy Calne FRS in interview with Dr Max Blythe
Trinity Hall, Cambridge 13 December 1996
Interview Three

MB Sir Roy, when we came to the end of our interview yesterday, we'd just got to the point where you were waiting to take a Harkness Fellowship in America, in Boston, but in the period of waiting, rather an exciting development occurred.

RC Well, it was exciting and disappointing. My boss, John Hopewell, was very enthusiastic about the experiments and he thought that the drug, 6-mercaptopurine, which I'd been using in animals was far better than irradiation, which I also felt, and that he would be agreeable for us to do a human transplant or even several. And we decided that, since we had nothing else to offer patients, this highly experimental procedure was something we could talk to a patient in a sensible way about and see what they felt. A middle-aged lady with polycystic disease of the kidneys, a congenital disease in which the kidneys are full of cysts and both kidneys usually stop working between the ages of forty and fifty, well she had reached the end stage. We didn't have regular dialysis as an option then, it was just something that was also being thought about, but we did have dialysis. She came in, and when we discussed it with her, she felt that this was her only chance and worth taking and we then waited for a donor. Now, also in those days, brain death was not a concept that was thought about or accepted and so a donor would have to be either a road traffic accident or somebody who'd had a brain haemorrhage where the heart had stopped beating and then the organs would be taken out as quickly as possible. So, a suitable case of brain haemorrhage, or what we thought was a suitable case, came in, a woman of about the same age, and we knew that she was going to succumb and got permission to remove the kidneys after death. I prepared the recipient patient for the transplant operation in one operating theatre, while John Hopewell removed the kidney that we were going to transplant in the other operating theatre. I was just ready to proceed when he came in through the door of the adjoining theatre and, although he had a mask on, he didn't need to say anything, his eyes just registered that something dreadful had happened. He said ' I've got the kidney here. Look,' and he lifted the towel off the kidney and it had polycystic disease, exactly the same disease from which the recipient suffered and, of course, both kidneys were the same and so there was no point in doing a transplant. We were absolutely devastated, as was the poor patient who died shortly afterwards. I've never forgotten the lesson that we learned that with polycystic disease, that there is an increased incidence of brain haemorrhage and we have always been alert to that possibility since. At the time, it looked as if there was providence against organ transplantation and this was a lesson that you shouldn't be dabbling in this type of work. I think we set up another case and did another transplant just before I left which worked for a short period of time and then the patient got pneumonia and sepsis which was, of course, and still is, a major cause of failure in transplants. And then when I went to America, Hopewell did another two or three, which were written

up in the British medical journals some years later. So, the first organ transplants with chemical immunosuppression, or the first attempts, were in fact at the Royal Free Hospital before the French and before the Americans, long before the Americans.

MB That Hopewell/Slome support you got at the Royal Free really got you started.

RC Without them, I couldn't. It's all right with a lot of opposition or indifference, but you must have one or two friends.

MB Not only were you up against a lot of indifference in your own profession, you were up against the great problem of rejection that really hadn't been pushed aside. That was the great challenge.

RC Yes. My other boss at the Royal Free was George Quist who was a very bluff and popular surgeon, but he felt I was doing too much experimental work and told the ward sister to watch me carefully lest I fill the beds with dogs instead of patients. That was typical of their attitude!

MB Roy, we're going to take you across the Atlantic now, first to New York. Can I first just get the family in perspective? You'd become a father by now, you had two daughters?

RC I had two children, one aged two and a bit and one under one year, two girls, and we travelled steerage in the Queen Elizabeth and met some friends, who we still have, on that boat.

MB And you played squash in the funnel, I think?

RC I played squash in the rear funnel. It's a very strange effect because you find the floor moving and the walls moving as you play and, of course, the local coach there, he knew it all, but we had to learn. It was fun to have some exercise. I don't think you can play squash in the funnels any more. We arrived at New York and at the Customs in New York the reception was extremely hostile. They didn't want any visitors and they feared everybody wanted to be an immigrant, and they opened every single piece of our baggage and we had these two little kids tired and hungry, and they opened everything and then closed it. We got through the Customs and then we were met by the Harkness people who took good care of us. These are fellowships which are very interesting, very good to have, because not only do they invite you to come and study, but they insist that you spend three months travelling and they give you a car for that. So after we'd spent a year at Harvard, we went three months travelling around America and did 15,000 miles, camping, and that was marvellous. But, they met us and took us to an hotel and I do remember the ambulances and police cars with their high noted sirens and my elder daughter, Jane, saying that there was a baby crying in the street, which happened quite frequently! Well, I had written to Drs. Hitchings and Elion, again at Burroughs Wellcome in Tuckahoe, New York, who had 6-mercaptopurine and had worked with the Boston group, Schwartz and Damashek, that's the Tufts group who had done the rabbit experiments. And I'd also received, in the meantime, a letter from Dr. Zukoski who worked with David Hume in Richmond,

Virginia, and he had started, also as a result of that paper, using 6-MP in dogs but found it rather toxic. We had some correspondence about dosage. He'd read my paper and was very kind enough to quote it in the Surgical Forum when he presented his data in the autumn of '60. Hitchings and Elion had said ' Why don't you visit us?' because I'd asked if they had something better than 6-mercaptopurine? It was not the perfect drug and, unfortunately, we still don't have the perfect drug. It was effective, but not perfect, and it had side effects which one didn't want. So they said, 'Come and spend a day with us and we'll talk about it.' There was a little train that went to the suburb of Tuckahoe in New York and I took that, and they worked in a big chemistry laboratory there in Burroughs Wellcome research, where they'd worked for years and been a fantastically successful team, Hitchings and Elion. And, in fact, they contributed not only to immunosuppression, but also to the treatment of malaria, to infectious diseases and some of their drugs were useful in the developing of anti-AIDS drugs later on. But, of course, their main thing was to try and have anti-cancer drugs, to stop cells from dividing. They were absolutely charming, very, very helpful and we discussed what might be good and what might not be good and Dr. Elion gave me a number of compounds that I might like to try in animals.

MB They were massively into producing compounds, derivatives of purines and pyrimidines?

RC Yes. They also took me to my first delicatessen meal in a little delicatessen in Tuckahoe which was wonderful, or seemed wonderful to me then. So now I had, in my briefcase, some compounds, new ones, and my wife and I and the two children took the train to Boston. We had already arranged where we were going to stay because it was in the same house that Dr. Ken Porter had stayed when he worked at the Brigham, in Wellesley Hills, a big old house where the owner was a real tough old Yankee engineer. He was a widower and he had left the house exactly as it had been when his wife had died twenty years previously. There was a coal-burning furnace to heat the house which I had to stoke, it was like stoking a furnace on the old war-ships, and my wife was housekeeper, which was in lieu of rent. So we were his English servants, as it were! But we had very nice living conditions there, apart from the fact that they were old, but not so old to us as to American friends who came and visited us. He was a teetotaller until we arrived and we completely changed his habits and before we left he was asking for his sherry wine, 'Where's my sherry wine, Patsy?' So, we did a lot of harm to him.

MB But, that was a nice domestic experience?

RC It was great, yes.

MB Roy, you meet Murray ...

RC Well, the day I arrived in Wellesley Hills, I phoned Dr. Murray who also lived in Wellesley Hills and he said 'Come over. We're just about to go on holiday for six weeks,' he was a great camper. ' We're going camping, but you can borrow our other car.' And that was a revelation because I don't think in England, well, people don't usually have two cars in England, but they're unlikely to lend you their second car just

like that without ever having seen you before. So, he lent us his second car and he discussed work.

MB He was your supervisor?

RC He was my supervisor and the department was Dr. Francis Moore's department. Francis Moore was an absolute giant in surgery. I think, by far the most impressive professor of surgery that I've come across anywhere. Tremendous intellect...

MB A great surgeon?

RC Well, he was more of an intellect than an actual operator, but he was a good operator. But, Dr. Murray said 'Well, you can join our irradiation programme.'

MB All you wanted!

RC And I said to him, 'Well, I've come all this way to get away from irradiation,' and he said, 'Oh yes, I've read your article in the *Lancet,'* – this was about 6-MP and prolonging kidney graft survival. So I said, Td really like to continue with that,' and told him I'd got some new compounds. I don't think he'd met either Dr. Hitchings or Dr. Elion at that time, but he said, ' Well, if you want to, you can do that work and then when I get back from holiday, we'll see how you're getting on. If it doesn't turn out, you can join the irradiation programme.' And I got an impression that although he'd read the paper he didn't believe it, or thought the results were unlikely to be repeatable, let's put it that way. So, I joined the lab where there were a lot of foreigners. There was only one American who had the Williamsburg flag outside his office to show there was one American in the lab, and the rest of us, mainly fifteen or so, came from all the world. It was a great community to work in.

MB A very different set of circumstances in America, a lot more freedom?

RC Well, there was a lot of money for research but, in fact, the laboratory was not particularly clean and one of the early experiments I tried to do was a heart/lung transplant and I sat up with the animal, as it were, in an ICU – it wasn't an ICU, it was an equivalent – and I was trying to take care of the animal all night. I was horrified to see sheep ticks climbing up the drip stand and then one or two jumped on to me. I was aware by then that they were around, and I got rid of them, but it was really quite dirty, the environment, and it was cleaned up very markedly a few months later. But initially, I was a bit disappointed because I thought that conditions were going to be much better than I was used to, because I'd been working at the Buckstone Browne Farm where, instead of a proper surgical light, it was an Ovaltine can with an ordinary bulb. Admittedly in Boston, at the Harvard Medical School, the lights were better and the equipment better, but the place was not all that much better.

MB Roy, while we're at this point, you've mentioned looking after animals and on a couple of occasions sitting looking after them overnight. You tended them, I know, with great care. You are an animal lover. How difficult has it been for you to actually

inflict pain and do a lot of work on animals? That can't have been easy?

RC No, it isn't. I mean, there are a whole number of ethical dilemmas that one has, transplantations have got unique ones, but if medicine is going to advance, then experiments have got to be done. Experiments on humans would seem to be completely out of court and the experience of the Germans during the War was so horrific, therefore one has to experiment with animals if one is going to learn new things. The animals are always anaesthetised and if they appear to be in pain, they are usually given an overdose of anaesthetic and put down. But it is a dilemma. I am particularly fond of dogs and yet I did quite a lot of experiments with dogs, but we did look after them as well as we could. My wife and I used to come at weekends to the Brigham Hospital kitchens and get the food that the patients hadn't eaten. The patients were quite fussy, I think, and hadn't eaten a lot of food. We were very hungry because we were quite poor and we felt that we would have quite liked to have had this food, but we gave it to the dogs instead. And we were able to take them for walks in the open air on the so-called sacred Harvard turf which wasn't very well kept, but it was a big green square outside the laboratories at the Harvard Medical School. I think it made a big difference to the animals to be taken for exercise and given titbits of really good food. One of the dogs escaped from the cage. It was a big Alsatian called Snappy, for good reasons. The day after the transplant he felt well and rushed off down towards the Fine Art Museum and we went off in hot pursuit, because we were worried what would happen to him quite apart from anything else, and we cornered him and he went under a stationary car growling and snapping, and we thought we were going to lose our hands in the process of trying to get him. A Bostonian matron was walking along with her dog that was a bitch on heat, and this suddenly took the attention of Snappy who came out and had completely forgotten about us, to this bitch on heat. This was the day after an operation, so he was a pretty strong dog, and we managed to get a lead on him and take him back. The Boston matron was very relieved that the bitch on heat was not sired, because it wasn't an Alsatian!

MB But your caring for animals went through all that. You minimised the problems as far as you could, but it was the way you had to go?

RC That's right.

MB And you did begin transplant work on dogs right away at Harvard?

RC At the Brigham, I used, first of all, 6-MP because I knew that worked, and then I used some other drugs. One of the compounds which is very similar to 6-MP, in fact it gets turned into 6-MP shortly after injection, is a drug called azathioprine, which is still used in transplantation. And when Dr. Murray came back from his holiday, I think he was very surprised to see a number of animals with kidney grafts that should have been rejected if they'd been treated with irradiation or anything else that they were using at the time, and so he felt that this work ought to be supported. Previously, I'd worked without a technician, but I think I was given two technicians then. In fact, I was given as many resources as I wanted. I think this was the big difference between America and England. No matter what the feeling was beforehand, if something was shown to be good and potentially workable and

important, then there were no restrictions on resources and help to do it. I was able to do all the experiments that I wanted to do, follow them up and didn't have to worry about investigations and the payment of it. Dr. Moore was also very interested and supportive. He was doing liver transplants at the time. He was pioneering the technique of liver transplants ...

MB He was using dogs?

RC ... dogs at the same time as Starzl was doing it in Denver. They were independent and both working on this ...

MB I don't think Starzl was having great success?

RC Nor was Dr. Moore. Both Francis Moore and Tom Starzl were struggling with a very, very difficult technique. I watched from a little distance all the work that was going on and I was not involved in it. I didn't want to spend my nights awake all night being ICU to these liver transplant animals. Dr. Moore recently dictated his memoirs and I went over to Boston and we talked together about it and he thought that I had actually participated in those experiments, but I told him that I hadn't. I watched them with interest.

MB You kept a close view on them?

RC Yes, but didn't actually contribute to the work at all, but I knew it was going on and knew what the troubles were. I was much more interested in trying to stop graft rejection, that was my main objective, and during that time I became friendly with the people at the Peter Bent Brigham Hospital, and there were some very impressive doctors there. There was Dr. Merrill, who was in charge of the renal side of things, and Dr. Hartwell Harrison who was the urologist. And the whole group, all of the doctors at the Brigham, were focused, at least all the departments had some focus, on transplantation. They were doing kidney grafts, then, between identical twins and an occasional transplant between people who were not twins using irradiation, and those all failed, although they had that one success between one set of identical twins. I remember watching an operation, and the American surgeons are very slow compared with the English surgeons or they were then. I was watching an operation which seemed as though it was going to go on forever and I met Dr. Merrill, who was the physician, in the corridor and he said ' How are they getting on?' And I said ' They're still diatherming the capillaries.' Anyway, this passed back and I didn't get any Brownie points for that remark!

MB Roy, can I just ask one question here? You were talking about the difficulties of actually technically doing the liver transplant work. Is that the actual surgery?

RC Yes, surgery.

MB That's the surgery itself?

RC Yes.

MB It really is quite a big operation?

RC No, the liver is less rejected than the kidney and in the pig, as I'll get on to presently, and the rat, the rejection may be self-limiting.

MB And while we're talking about liver and kidney, I mean, you essentially had specialised, set your mind around the kidney work, that was where you were at, although you've mentioned heart/lung interest?

RC My interest was then, and still is, primarily in the biology of transplantation and not in any special organ. But the kidney was the obvious first organ to transplant because there are two of them, so the patient can do without one. There's dialysis as a back-up if the kidney doesn't work immediately, and the actual surgery is straightforward, nobody argues about the surgery. Well, there was one argument I do remember. I was assisting Dr. Murray with doing an identical twin and there were two veins, renal veins, on the kidney, usually there is only one, and he couldn't join up the second one which was small and decided to tie it, and the patient did very well. If you tie an artery to a kidney, that portion of the kidney supplied by that artery dies, so the veins and the arteries seem to be different. So, I said I'd do some studies on this because we had a long discussion about it, why did it do well, and we did, we thought, quite elegant injection experiments to the veins of kidneys, human kidneys, and found that there were, in fact, many interconnections within the kidney. We had nice pictures of this and we were prepared to write it up and were going through the literature, when we found there was a reference to the veins in the kidney by John Hunter, in the eighteenth century, in 'A Treatise on Gunshot Wounds', a book he wrote, and we were absolutely amazed to read that Hunter wrote 'as for the veins they join one to another in a wondrous manner'. So it was all in the literature for 200 years!

MB Roy, while we're thinking back to that period, 1960, that was a time when Barnard was around and various heart transplants had been tried, chimpanzee to man. That was a fascinating time surely?

RC No, in 1960, the only heart transplant work being done was by Shumway. Barnard hadn't surfaced at all at that stage. Shumway was doing experimental heart transplants, only experimental, not in man. There wasn't much else going on, except the kidney.

MB So, you were in the thick of where it was at?

RC Yes, the Brigham was the place where the first kidney transplants in man had been done as a proper series by Dr. David Hume, whom I met while I was over there. He was by now at the Medical College of Virginia in Richmond, a wonderful person, a tremendous surgeon with tremendous intellect. He'd done that work in Francis Moore's department before he got his Chair.

MB But, before you got there, they'd been into x-radiation like there was no tomorrow. You introduced chemical immunosuppression?

RC That's right.

MB Can I push that point, because they have never really acknowledged that, I think?

RC I think in Francis Moore's book which he wrote, 'Give and Take', he gave a very truthful analysis of the history of it, but I think they felt a bit rueful that they hadn't done it earlier because Bob Schwartz was down the road at Tufts in their own town. But the use of it, and the demonstration that it could work in organ transplantation, I had done in England, and there is a tendency in America to feel that anything done outside of America needs to be repeated and treated with suspicion. But, it's acknowledged perfectly fairly by Dr. Moore.

MB But not by Murray?

RC Oh yes, and by Murray, but it's interpreted by others in a different way. Oh yes, definitely by Murray. What happened was that it took my whole time in America to really convince the sceptics, everybody was a sceptic, but the sceptics who mattered, denied that this might be better than irradiation. Since irradiation was one hundred per cent lethal, apart from non-identical twins, it didn't have to be much better to be better than irradiation. And my work really set the stage for doing it in man because until the definitive experiments had been done in reasonable numbers, it wasn't regarded as an acceptable thing to do in man. At about the time I left, the first transplants were done using azathioprine in man and that point has always been looked at as the point of use of immunosuppression in organ transplantation whereas, in fact, it was nearly two years after it had been used at the Royal Free in England. I think there is a natural, well, I don't know if it is natural, but there is a tendency to look at it that way. I did, in fact, publish the first use of azathioprine in a fairly extensive paper in the journal, called *Transplant Bulletin* in those days, later to be called *Transplant*, and that was just in my name. Dr. Murray was the co-author of a presentation to Surgical Forum afterwards, and my publication is never cited, but the one with Dr. Murray is always cited. I just wonder whether that's a Freudian slip, that they forget about, the one in *Transplant Bulletin*, which was a more analytical explanation of the work. But, these things happen in the sciences, there are so many precedents for it, it's almost par for the course.

MB While you were at Harvard, did you teach in the medical school?

RC Not really, no. I did a little bit of teaching and joining in teaching with the residents, but I was involved primarily as a research fellow.

MB You had one or two enormous successes with dogs who kept their kidneys for long periods?

RC Well, there were quite a number, but the first one that did well was a cross-collie dog called Lollipop who was everybody's pet, and she was allowed to roam freely everywhere in those days. There were no restrictions on experimental

animals. Once a week they had grand rounds, and still do in all American teaching hospitals, and it was decided that we would present this dog as a case. So, the chief resident read out the history of a young adult female without any kidneys who'd received a kidney transplant and was treated with this new drug, azathioprine, and now at six months, or whatever it was, kidney function is normal and the patient is doing very well. And he said, ' Now, Dr. Moore, may I bring the patient in?' Dr Moore knew exactly what it was all about and said ' Yes,' opened the door, and Lollipop rushed in to the amphitheatre. I don't know if there had ever been a dog in the amphitheatre before, probably, but nobody could remember it, and she rushed up and down the front row looking for me, I think, but she was licking all the professors sitting there in the front row and made quite an impression on everybody who was at that particular ground rounds. In fact, that was what probably tipped the sceptics to say ' Well, maybe we should use this.'

MB Right, coming back to England now, to St. Mary's. I think there was a contact that you had made while in America, Bill Irving?

RC Bill Irving was one of the visiting professors. In fact, I made lots of English contacts because they all used to go to the Brigham in those days – and so, although I had been told that I would never get a job in England again because I'd gone to America before I was a senior registrar, I was only a middle-grade registrar, I had several offers of jobs in England and also in America. One really attractive one was at the Johns Hopkins by Dr. Blaylock who was one of the leading surgeons in the world at the time, and had come and visited us and had seen the experimental work. But Bill Irving, who was Professor at St. Mary's, offered me a job at St. Mary's as a lecturer, a senior registrar, and so when we came back to England, that was the job I had. But, before that, we had this three month trip around America which was absolutely fascinating. Dr. Moore had written to his colleagues and friends in various cities where we were travelling to and so we were in a tent with the kids and the next morning I would put on a suit and go into the Medical School and give a seminar on immunosuppression. Then I'd get back to the tent in the evening and cook the soup. It was a wonderful existence actually.

MB Yes, sounds terrific! In that time, I know you were doing quite a lot of camping as you made clear and seeing some quite beautiful tracts of America, were you actually sketching and drawing at that stage? We know the love of art was there?

RC I don't think I did any drawing then. I mean, I have, as you know, painted since I was a child, but I didn't do any sketches on that trip which is a great shame, because it would be nice to look back on them now.

MB You were a busy dad with plenty on.

RC Well, I was also trying to be a tent lecturer which is a bit unusual, but I was treated extremely well in all the Medical Schools I went to. I suppose, Houston was where I don't think I was treated so well, but others did. I went to DeBakey's unit. I watched Cooley operate and I was really impressed with this fantastic surgical technique. Then the next day I was going to watch DeBakey operate and got to the

operating room and was ushered away from it, so I showed Dr. Moore's letter, and they then put me in a viewing gallery right at the top, miles away, so I wouldn't disturb in any way the great DeBakey. Everybody was terrified of him in those days. They called him 'Black Mike,' and he had a dreadful temper in the theatre, and anybody who crossed him, their career was just utterly finished. He hadn't arrived then. He was coming in on an overnight plane and then immediately going to the operating theatre to operate, so it was suspected he wouldn't be in a very good mood. Any rate, he was doing a big aneurysm, a big vascular case, and eventually he looked up and asked who I was and somebody told him that Dr. Moore had written and he remembered. So I was ushered down to the operating room floor and told to look at, but not touch, all the things that he was doing, and then I was whisked away. I had minders around so that I wouldn't upset him and make him in a foul mood. I went to the coffee room and had a coffee and one of the residents came in and said, ' What did you do to get that red carpet treatment?' That was my contact with DeBakey at that time.

MB That was a memorable trip to America?

RC It was a memorable trip because we went everywhere. We did 15,000 miles and went into most of the national parks, and into Canada. We had a very generous visit with Shumway in Palo Alto and he was just about to use azathioprine in dogs with heart transplants, having heard of the work with kidneys. Then we went to Seattle, where Scribne was doing regular dialysis as a form of treatment, and he was also a very generous host. I met Robert Good, he was in Minneapolis, I think, and he and Miller were the two who described thymus and thymus-derived lymphocytes, which were an extremely important concept in transplantation immunology. I remember he had a minute little office and he told me he thought that it was a good thing to do good work if you didn't have a good office. He was also very charming and interested in the work that I was doing. So, that was a great trip around the States and then we came back. I'd warned my wife that it was dangerous to go camping for three months with two little children and that they might get ill, but the only person who got ill was me. I can't remember what, and I wasn't very ill. I think I had glandular fever or something like that.

MB You came back and it was all fixed for you to go to St. Mary's by then.

RC By then I had a job at St. Mary's and I went there. Irving was anxious for me to do kidney transplants, I think, to take it away from the other surgeons who were doing it and had one hundred per cent fatality with irradiation. They didn't want to change. Nobody ever does want to change, but when it was pointed out to them by Stan Peart, who was Professor of Medicine, that their results weren't very good, that they couldn't be worse, there was reluctant agreement to change to immunosuppression and we started to get some better results. They weren't marvellous, but we started to get better results. I wasn't at St. Mary's very long before I went to Westminster.

MB Before we go on to that, Roy, that link with Stan, Ken Porter and Bill Irving, that was a strong team you made in that short time you were there, they were very

supportive?
RC Well, Stan Peart and Ken Porter were certainly supportive. I think Bill Irving needed to be supported most of the time.

MB There was a lot of feeling about you coming in with new ideas in the surgical field, the other surgeons ...

RC ... they didn't like it, no. The surgeons who were already doing the kidney transplants thought this youngster is coming to usurp us and tell us what to do, and whilst we're not getting much success, he thinks he can do better.

MB I just wanted to clarify whether you were glad to go to Westminster because of that opposition to some extent or whether Harold Ellis was ...

RC Both. I think Harold Ellis was going to provide a higher level of support and interest. Stan Peart was a good support, but he wasn't a surgeon, and Bill Irving was interested in other things really. He wasn't interested in transplantation primarily.

MB When we went to St. Mary's to record with Stan Peart, he showed us little boxes that you'd built, little cubes for patients in some of the wards, I suppose, to reduce the risk of infection. We actually saw those. We've got those on some of the footage of video tape that we've got. Let's go now to Harold Ellis.

RC Well, Harold Ellis I had known in Oxford where he was the surgical tutor and he used to teach for the fellowship examination which I was taking. He must be the best surgical teacher in a space of about forty or fifty years. He and Slome were both natural teachers, loved it, and both to some extent actors as well as teachers. They really loved an audience that responded to them. I enjoyed his rounds, and benefited a lot from them, and then it was good to work in his department and he got me immediately to write a book with him 'Lecture Notes in Surgery' which is now in its ninth edition. The junior lecturer was Chris Wastell and the in-between was Norman Browse, currently President of the Royal College of Surgeons, and I think it was a pretty strong team, each with different interests, and I was able to continue with my experimental work and do the beginnings of clinical work. But it was very difficult to do clinical work there, anywhere really, because of the general distrust of the whole idea of transplantation by medical and nursing people. The nurse in charge of the operating theatres at Westminster wouldn't have a corpse in the theatres, so we had to remove the kidneys from patients who had died in the ward.

MB In the wards?

RC And the wards were big open wards with maybe twenty or thirty people in them, and the poor patient who'd died, they'd pull the blinds around, and then we, using an ordinary light, were trying to remove organs from a dead person in a bed. We would normally operate on someone on a rigid surface which doesn't give, but inevitably there would be blood dripping on the floor and the other patients would see it, and the whole thing was utterly macabre. I don't think anybody could believe what happened and eventually the complaints at this procedure even forced the theatre

sister, who was extremely powerful, to give way on this. I also remember removing kidneys from people who were dead in an ambulance which, I suppose, was just a little bit better and more aesthetic than in bed in a big ward. But, we really did do that, that was literally true. We had one or two patients that did well. A lot didn't, a lot got infected or rejected, but whilst I was at Westminster in 1963, there came a report from America by Keith Rheemster that he had transplanted kidneys from baboons and chimpanzees to man, and Starzl then did some baboon to man and Hume did too. It wasn't very much after that that Hardy did a chimpanzee to man heart graft, and I felt that this was going to be the future if it worked – and the early reports were very encouraging- as it would take away this very difficult and worrying business of removing organs from corpses. So I managed to get some kind of grant to go to America and went and met Keith Rheemster in New Orleans and saw monkeys being wheeled on trolleys into the operating theatres with little operating hats on and looking most bizarre. I saw a lady who had had a chimpanzee's kidney which was still working at seven months and went on for nine months, and so it looked as if this was going to be the thing. But in fact that was the best result and there were no long-term survivors. The best result was from chimpanzee to man and, of course, chimp is very close to man. I think ninety-eight per cent of the DNA is the same, but even then rejection couldn't be prevented. So, I became a little bit disillusioned a short time later, but I went back to England and thought I must do some work on grafting between animal species and also wondered what about primates to man and met Oliver Graham-Jones who was Chief Vet at London Zoo and he said ' Well, I will be of any help I can. I'm very interested in this.' My beds were at the Gordon Hospital, part of Westminster Group, in Gordon Square, near Vauxhall Bridge Road, and we decided to have a room there that was going to be sterile, and that if we were going to have animals as donors that there would have to be some way of handling the animals so that we could control them, also, so that they didn't hurt us. We thought we'd do a trial run and we had a dogura(?) baboon, which are very big animals, about this big, with a face like a dog and teeth about an inch and a half long, canine teeth, really fierce. And this baboon arrived at the Gordon Hospital asleep and he was moved, anaesthetised, to this cubicle actually in the ward of the hospital. You can imagine doing that now. And the baboon decided to wake up when he was just settled in bed under his anaesthetic and everybody fled screaming and Oliver Graham-Jones bravely went in with a syringe and gave some more anaesthetic, and these dreadful teeth were gnashing! So, we never did a transplant, but we did have an anaesthetised baboon in the Gordon Hospital, and that was as far as we went with xenografts at that time. (The baboon went back to the zoo).

MB But the animal work continued alongside some kidney grafting in those periods at the Westminster, 1962 to 1965?

RC Yes.

MB You had some rather nice colleagues who were supportive there. I think you had a number of surgeons in support of what you were doing?

RC Yes. Well, junior ones especially. My registrar and senior registrar were certainly supportive. Harold Ellis was supportive. Malcolm Milne, who was

Professor of Medicine, a very brilliant physician, he was initially very sceptical but eventually came on board, and Lavinia Loughridge, who was the Senior Lecturer in Medicine, was a very good colleague, and so we were able to proceed in a slow, steady manner.

MB You found these a very good three years?

RC Yes.

MB How did the kidney transplantation in humans go? Was that improving? Were you getting better results?

RC We were getting better results. They weren't very good, but there were some patients that went a long time. I think one patient went several years. I think one went about ten years because the patient used to come and see me in Cambridge.

MB So, you began to feel a sense of fulfilment seeing this development actually advancing ...

RC Well, we knew it could work, I think. We knew from the twins of Murray that the kidney could be transplanted surgically, that it could work a long time very well. We knew that it was possible to suppress rejection, but difficult. There was a kind of two-pronged worry of rejection on the one hand and infection on the other. It was difficult to sail that channel between the Scylla and Charybdis of those two opposite disasters, and I felt all the time that we've got to get better immunosuppression. We were using corticosteroids together with azathioprine then, and some of the early patients are still alive. My longest patient is thirty years now post-transplant with an unrelated cadaveric donor. That patient was transplanted shortly after I came to Cambridge.

MB Just thinking of that coming to Cambridge, towards the end of that period, when you were consultant and senior lecturer at Westminster, you started to feel that a Chair was right and began to look at one or two professorships internationally and nationally and got an offer to go to Melbourne, I think?

RC I went to St. Vincent's in Melbourne which is a very fine hospital and I went over as a visiting professor and they worked me almost to death, but fortunately, I had a game of squash each day to resuscitate. My wife was taken on the harbour, she was taken sailing, she was taken to see koala bears .....

MB And you took a larger family there at that stage, I guess?

RC We didn't take the children. No, we left the children with my mother.

MB But it was a slightly larger family by then. You'd moved ahead slightly by 1965?

RC Yes.

MB You were building quite a family?

RC That's right.

MB And that was really an enjoyable part of your life. I mean, we've got the whole pressure of the search for tolerance and grafting success, but there was a family life at home that I don't want to lose sight of because ...

RC Well, I think I had! My wife said she never saw me and I didn't have any of the worries of the children because she looked after them when they were ill and so on, which is all absolutely true, because I was not only doing experimental work and trying to do transplantation, but I was also doing general surgery which, of course, I still do.

MB But, they were the important foundation of your world, whether you saw them or not?

RC Without doubt they were, but I don't think I fulfilled my role as a father in an acceptable way, but something has to give. There's not enough time to do all these things, if you want to do them.

MB The Melbourne job offer eventually you discarded in favour of the Cambridge Chair. I can understand that, I mean, you preferred to stay in England. Was that appointment easily arranged? Did you come to Cambridge without too many difficulties?

RC The Cambridge Chair was advertised. They didn't always advertise Chairs in those days, they would go and seek the best person and if they didn't find the best person, they advertised it. Cambridge academic jobs paid less than other universities even in England, so there wasn't a tremendous rush of people to want to do the job. I wouldn't say I got it entirely by default, but there wasn't a huge number of people seeking it, and Professor Mills here seemed to like the idea of a new subject, transplantation, coming to Addenbrooke's. I think he was entirely alone on this. I don't think anybody else wanted it.

MB So, he was the visionary in that context?

RC Definitely, without any doubt. It was he who had the biggest say in the Chair. Addenbrooke's had a cottage hospital mentality then and he had a lot of difficulty coming from London and setting up a Department of Medicine, and I think he wanted an ally who would share the flak a bit.

MB You came to a small department?

RC Well, it was incredibly small, yes. I had a secretary without a typewriter, a room over a dwelling house near Addenbrooke's where there was an Indian family underneath, so we had a continuous odour of very powerful curries which I was quite

used to after the Gurkhas, but my visitors thought was a bit strange, and I had one lecturer. It wasn't a department really, it was just a few people struggling to get hold of a typewriter for the poor secretary.

MB So, you came here with an interest in getting the transplant surgery going, but with general lists to look after and the main thing was to continue the animal work and to look at the rejection processes?

RC That's right.

MB What was it like. I think you must have tried to make contact with the Vet School?

RC Yes, the vets didn't like me, I don't think they do still, but they didn't want surgeons coming in. They felt threatened I think, although they did give me some outhouse which I converted into an operating theatre, but at the Agricultural Research Centre in Babraham, Richard Keynes was head of that at the time. He was a man of foresight and he had a wide-ranging interest and thought this would be good work to do there.

MB So, they welcomed you.

RC And they gave me facilities and charged almost nothing, although by that time I did have some kind of a grant. It is interesting that when I was at Westminster, I was trying to get some money to do experimental work and wrote to the MRC and, instead of a whole book full of forms to be filled in and peer review and a tremendous, really time-consuming and effort-consuming business of getting a grant, Harold Himsworth, who was secretary of the MRC just came down to the Gordon Hospital and had a chat with me and went through the experiments and said, well, this probably won't be successful, but it looks quite interesting, so we'll give you a couple of thousand pounds or whatever. That was the way in which it was done in those days. Going back to Babraham, the main animal species to work on there was the pig. The immunologist, a vet who had just done a PhD in immunology called Richard Binns, had repeated Medawar's experiments of tolerance in the pig. He had opened the uterus of pregnant pigs and delivered the foetus, injected into the foetus cells from another pig, and then closed the uterus again and these animals he would then skin graft. And he found that the skin grafts were accepted for long periods of time, but most of them were eventually rejected. So, there were some very important lessons in transplantation that I was slowly beginning to learn. One was that skin and kidney are different and another was that species are quite different and what you learn in one species may be inapplicable to another. And because he had these animals that had been injected *in utero* and the donors were still alive, we did some experiments of kidney transplantation into these semi-tolerant animals and the kidneys were accepted, whereas the skin had been slowly rejected. I had, before I went to America, when I was at the Royal Free, done some experiments of kidney grafting between non-identical cattle twins which, of course, was where it all started with Medawar, and those kidneys were not rejected. So, I was able to work closely with Richard Binns. Our interests were entirely complementary, and we did a number of

experiments together for a long time actually, because then we became interested in the liver and it must have been in 1965 or 1966 that there was, I think, a Surgical Research Society meeting in Bristol. Joseph Peacock and John Terblanche, who was his research fellow, had been trying to do liver transplantation in the pig using Francis Moore's or Starzl's method and they had one pig that had lived a very long time. They'd been preceded in this by a French surgeon [Gamier] who had also had a pig last a long time with a liver graft and when I saw this, I was just amazed. It didn't seem to interest either the French group or the Bristol group as much as it interested me, maybe because I had been wrestling with rejection, usually unsuccessfully, already for some years and they were more interested at the time in the actual technical side of transplanting the liver. So, since we had superb pig facilities, I decided that it would be very interesting to study this immunology of pig liver rejection and why the pig's liver could last for a long time, and I taught myself to do liver transplantation in the pig. It took a bit of time, but once we had the experiment going well it was easy to show that some pigs rejected the livers quite quickly and other pigs didn't. They went through a rejection crisis which then got better on their own and then they were tolerant, and one pig lived for eleven years without any drug treatment at all. This was quite unprecedented and since we were able to do kidney transplants as well, we did kidneys from the donors as well as livers at the same time, and found that the liver would protect the kidney. This was, really, the beginning of a new major research interest which continues to the present day. We haven't been very quick at solving it.

MB The way in which the liver confers a degree of protection?

RC Yes. Well, I mean, complete protection in some species. Unfortunately not in man. But, having the technique well developed with reproducible good results, technically, it seemed that it would be sensible to look at liver transplantation in man.

MB And a chance came in '68?

RC Yes, because Starzl was beginning to publish results which were very bad, but with an occasional good long-term survivor. I think the first two or three liver transplants in man that I tried were to put an extra liver in the patient and that seemed to me was going to be less of a trauma to the patient than taking out the patient's own liver and putting it in the right place. I am sure I was mistaken in that, because it's difficult to fit an extra liver in, it's an irregular organ, and it fits best in the correct place. The first liver in the correct place that we did was in, I think, March or May 1968, because Dr. Moore from Boston was visiting Cambridge at that time to see his son who was doing Molecular Biology, and he phoned me up and said, 'How are you getting on? I'd like to come and see what you are doing.' So, I said, ' Well, today actually, is a good day to come because we want to do a liver transplant in a patient, and there is a donor where the parents have given permission, but there's a lot of opposition in the hospital and we're going to have a little meeting to discuss this.' We had this meeting in the old Addenbrooke's and the case of the recipient was presented and the demise of the donor was presented, and then all the people who might be involved, anaesthetists, surgeons, theatre staff, laboratories, they all gave their verdict, and it was universally negative. They each had different reasons, but nobody wanted to do it. They were worried that the virus in the child who had died would

spread to the recipient, worried that we weren't yet ready, worried that the recipient was too ill, worried that the recipient was too well, every possible objection and, actually, I'd met this all before with the kidneys at St. Mary's, also at Westminster, so I was expecting it. But it was very vehement and a very solid front, although the reasons were different. Then I introduced Dr. Moore and some of the people had actually heard of him and I said, ' I think we ought to hear him,' because he was one of the pioneers of experimental liver grafting, and Dr. Moore spoke very shortly and said ' There can be no doubt that this is the most perfect opportunity to proceed and we've got to do it.' And I think that evening we actually did the transplant with Dr. Moore as the first assistant. I've got the operation notes and you can see that Dr. Moore was first assistant on that.

MB He smoothed the way for that. Everybody went with it after that?

RC Yes, he broke the opposition completely.

MB Tremendous.

RC Well, nobody I think felt they had the intellectual capacity to argue with him, and they were right too, they didn't!

MB How long did that graft take for?

RC The patient lived about two months, I think, and died of an infection with the liver still working, and we were initially delighted because the operation went well and was working and the patient woke up. The failure in all kinds of transplants has been either the immunosuppression is insufficient, resulting in rejection, or too much immunosuppression, resulting in infection. There's always been a very, very narrow gully to go between, like parking a car where there isn't quite enough room.

MB You continued with liver transplants from that point. I know you've done eight to nine hundred now, I should think?

RC Well, we have done more than one thousand, and I personally have done, I don't know how many hundred, but something of that order perhaps. But, we had a weakness in this programme after doing the first few, because we had no hepatologist in Cambridge. Dr. Roger Williams had been a colleague of mine at the Royal Free, we were both registrars. I think he was the senior registrar and I was a registrar. He was with Sheila Sherlock who was Professor of Medicine at the Royal Free, and was a hepatologist at Kings College Hospital in Denmark Hill, and I phoned him up and said, ' Look, we've started to do liver transplants, we have no hepatologist, how would you feel about joining us?' So that was the beginning of a collaboration for twenty years, where the medical side was done by him and the surgery by us, both in both hospitals, and we would go down and do the surgery sometimes in Kings and he would come up to Cambridge and look after the patients and send his residents to look after them in the ICU. This really worked extremely well for a long period of time until King's got their own surgical side, and then we were in trouble until we appointed our own hepatologist.

MB I think we're overrunning our time, but that wasn't until the late eighties or sometime like that. They pulled out rather suddenly, and I think it left you a bit of a gap, Roy, and that was not comfortable after a very close association. Am I right about that?

RC That's right, yes.

MB So, you had to develop hepatology here very quickly?

RC Yes, we didn't do it quickly, but...

MB Had to do your best. Roy, staying with those early years in Cambridge and the developments, the kidney transplant went on, the animal work continued and the Babraham side was the key side of your research. The work with Richard Binns was seminal; the liver work went on. There must have been a great break around 1977 when cyclosporin A came into the story. That must have been one of the next big steps in the journey we're looking into?

RC Yes, when we weren't studying the liver, we were trying to prevent rejection by different methods, different drugs or different manipulations of the immune system, and getting uniform results which were unsuccessful. I think, it was in 1977 when a Greek surgeon, Dr. Kostakis, had been with me for nearly two years and who was very popular, but didn't do any work – he enjoyed Cambridge – came to see me and said, ' My Professor will be angry with me if I return without having done any work.' I said,' Well, you have had every opportunity, I can't spoon-feed you, I can give you the chance to do work, but you have chosen not to.' So, he said ' Well, I must do something in the last few months.' So, I said, ' Well, what do you want to do?' He said, 'Well, I want to study immunosuppressive drugs,' which I thought was a fantastically new idea since it was what we'd been doing for the last twenty years! So, which drugs? He said he didn't know. So, I said ' Well, you'd better first get the model going of heart transplantation in the rat.' That's putting an extra heart in the neck or the abdomen of the rat. And he came to me and he'd worked very hard and he said ' I can now do it.' So, I said ' What drugs would you like to do?' He said he'd like to look at the ones we were already using and David White had heard Borel. Borel was the person who discovered cyclosporin and discovered that it was immunosuppressive, both *in vitro* and also in animal experiments, it prolongs skin grafts, and so David said ' Well, why don't you try Borel's drug?' So, Kostakis burned the midnight oil, literally, and came across trouble in the first place because cyclosporin wouldn't dissolve. He couldn't get a uniform dosage and he didn't know how much he was giving to the animals. It would dissolve in alcohol, but it's difficult to inject alcohol into animals. But his mother had been worried about him in England, starving to death with the rotten English food, and she'd sent him big cans of pure first quality Greek olive oil and he found that this was a marvellous solvent for cyclosporin and, once he used the olive oil, he started getting great results and he came to tell me about them, I remember when I was in one of the patient's rooms watching the semi-finals of Wimbledon. I couldn't get down to Wimbledon, but I was watching it on the television. I told him to keep quiet until the end of that set and then

he told me these results and I said, 'That's extraordinary. Are you sure about the strains?' He said 'Yes, absolutely sure.' I said, 'Well, you'd better go and repeat it because it sounds too good to be true.' A few weeks later, he came back and said, 'I've done some more experiments and the results are just as good or better.' So, it was at that time that I thought this was a fascinating drug, we all did, and I phoned up Sandoz and asked them if we could have some cyclosporin to study in large animals, in pigs with heart grafts, which we knew were rejected and, by this time, had learnt the technique of heart transplantation which was another new organ transplant to learn, and in dogs with kidney grafts. And they said, 'We've stopped working with it. It's no longer on our books for development.' And I said, ' Well, the results are really very encouraging.' So, they said, ' Well, we've got some in the lab, we'll send it to you. See how you get on with it.' When I started to get good results with the dogs and the pigs – the pigs with the hearts were the best, they became tolerant after giving them cyclosporin for some months and rats also became tolerant, dogs more difficult. Dogs have always been more like man, more difficult. Then David White and I were invited to Sandoz in Basle, and I was asked if I would give a seminar on it. I think, by this time, I had already done the first patients with cyclosporin and I was very disappointed to find that, in man, cyclosporin is nephrotoxic. In fact, some people didn't even believe this. But, in animals we never saw any evidence of damage to the kidneys and it's interesting because, if you look at it from the other way around, if it had been nephrotoxic in animals, we would never have used it in man and we'd have never known about it and if it had happened to be non-nephrotoxic in man, we might have missed it, so there may be a number of drugs hanging around which have never been used. But, the Sandoz people listened to my talk and then they had their own private discussions and decided to develop the drug for transplantation. They decided to do it to try and get, as it were, good marks for the non-profit attitude of Sandoz because it was very expensive to make. The market they thought in transplantation was minute, and that developing it was going to be a loss to Sandoz in terms of money, but a gain to Sandoz in international recognition of their altruistic attitude to drug development. They entirely miscalculated, as did everybody else, that cyclosporin would create its own market, because the results improved so much that people were developing transplantation clinically all over the world. For the first time, it became possible to transplant the liver and the pancreas and the lungs and the heart with reasonable results. Previously, there'd been a few odd good results. Kidneys had been better with azathioprine and steroids. But, here was a kind of quantum improvement...

MB Which changed the whole quality of life for children who'd had transplants?

RC Because they didn't need to have high doses of steroids. I wouldn't transplant children before that because I was upset by the stunting and Cushingoid effects of high dose steroids in kids. So, it was, really, a watershed. It transformed organ transplantation from a practice of a few wild and possibly mad surgeons to a kind of therapy that everybody wanted.

MB And David White in your department, I think, showed some of its significant effects on macrophages, is that right?

RC He started that because we thought that that might be its action. It isn't

actually effective in macrophages, but that was our first line of thought to be working on macrophages, that's quite right. He directed much of the work in developing and doing the laboratory studies of cyclosporin, but the main breakthrough observation had been made by Borel, there's no question about that, in my opinion. They argue about it in Sandoz and I think it was Borel, but he couldn't sell it as an idea. He had great difficulty in persuading people that it was a great drug and I think Kostakis' experiments were very important. Also, Green and Allison, working at Northwick Park, did work at the same time as we did in kidney grafting in rabbits and although Kostakis's paper was the first to be published in a medical review journal[1]. The more definitive paper in dogs and in pigs and in rats was published in the *Lancet*[2] in the same edition as Green and Allison[3] from Northwick Park. They haven't had much recognition of that. Still, it was the observation of Borel that was the turning point, I think.

MB And Kostakis went back to his homeland with a transformed reputation.

RC Yes, his professor was very pleased with what he did in those three months.

MB Roy, just looking at the unfolding from the cyclosporin A story, were there more and more improved developments using that technique. You said that was a great watershed. Was that the story of the 1980s?

RC Yes, I think that we had no idea how to use cyclosporin to begin with and we gave much too much. We gave the animal dose translated to man and man doesn't tolerate so much. Man tolerates about one-third of the dose and how were we to know that? Well, we didn't, and we got it wrong. And then we found that if you combine cyclosporin with Imuran [azathioprine] and a small dose of steroids, you could give much smaller doses of all the drugs, but they would give additive immunosuppressive effects, and each have different side effects. I think that was an important concept of combining drugs with cyclosporin as a kind of sheet anchor drug.

MB So, the Cambridge department continued to publish heavily on those techniques, these pharmacological approaches?

RC Yes, but we weren't alone. All over the world there were important publications on this.

MB You mean, now it was a growing field?

RC Yes.

MB One thing we haven't put on the map is that I think people often think of you

[1] Kostakis AJ, White DJG, Calne RY. (1977) Prolongation of rat heart allograft survival by cyclosporin A. *IRCSMed. Sci.* 5, 280.
[2] Calne RY, White DJG, Rolles K, Smith DP, Herbertson BM. (1978) Prolonged survival of pig orthoptic heart grafts treated with cyclosporin A. *Lancet* 1, 1183-1185.
[3] Green CJ, Allison AC. (1978) Extensive prolongation of rabbit kidney allograft survival after short-term cyclosporin A treatment. *Lancet* 1, 1182-1183.

as a kidney and liver man, but you've had quite a lot to do with heart transplantation, Roy?

RC Well, I was interested in heart surgery, having worked for Brock in the early days, and I was also interested in the techniques of heart/lung bypass because bypass was one of the techniques used in liver transplantation, some form of bypass. And it seemed that Shumway was getting results, after Barnard did the first human heart transplantation, he really took the experimental work of Shumway into the clinic, which was a brave thing to do, and Shumway had been unable to do it as there was too much opposition to it. But, once it showed that the hearts were doing reasonably well and then when we had cyclosporin, I felt that we should be doing heart transplants in Cambridge, and I did about five hundred experimental heart transplants in all, in pigs. I studied preservation of the heart and would have liked to have done heart transplantation, but the logical thing really was to do it where they were doing human bypass every day now in places like Papworth. So, Terence English was appointed. He was interested, he joined my experimental group and then he started the programme of heart transplantation in man. I wanted him to use cyclosporin because we had just shown it was so much better in the kidney, but he wouldn't, he wanted to use the traditional azathioprine and steroids. We would have been the first to have used cyclosporin in heart transplants, but he didn't want to do that, and so Shumway did the first cyclosporin in man, in heart transplants, and showed that it was much better.

MB So, they got there first?

RC Yes, but the most important thing was that we had the drug which had been used in man.

MB There's one small story I've neglected relating to your early days in Cambridge and that was that you met up with John Butterfield again?

RC Yes, John Butterfield became the Regius Professor of Physic in Cambridge. He had been a cricketer ...

MB And you stood in for him all the time!

RC ... and he'd also had my brother in his department at Guys, so there was common ground there, and he was very supportive of my work, always was, and also tolerated my hatred of bureaucracy, particularly of committees ...

MB Yes, he started to stand in for you, as a return favour?

RC Yes, I think that was only fair. He said, ' I know you hate committees, Roy, and don't want to go to any of them and as far as I'm concerned you don't need to go to any of them unless I give you a three line whip that you've got to come and I really need you. Otherwise, I'll support your interests at all the committees.' So, I hardly went to a committee, and I think that really saved me from ...

MB Enormous wear and tear!

RC ... well, no, it permitted me to do some work, some useful work. We have created an extraordinary structure now, whereby filling in forms and peer review and committees have almost succeeded in stopping any progress. I suppose that's what people want. They don't want any progress. With that, and with the Animal Rights, I think it's not surprising that academic surgery is much less popular now than it used to be.

MB I think there was a period when you had a lot of trouble with Animal Rights, Roy?

RC Yes, yes. They persecuted me and my family. They sent me a bomb, they used to give telephone calls every day and asked my wife what it was like to be married to a murderer and a torturer. And then, when we did a transplant on a child, Ben Hardwick, which had national publicity, when Esther Rantzen's programme 'That's Life' took up the plight of a child needing an organ donor and it was successful and we did a transplant in Ben, the Animal Rights people seemed to get off my back, me personally, and I've not had much trouble. I'm sure they don't like me, but I don't do so many experiments now. I don't think that's the reason they got off my back, but I think they felt that attacking someone who was trying to help children was not a very good publicity stunt.

MB We also said in conversation earlier that the programme 'That's Life', that promotion by Esther Rantzen, brought more donors on stream.

RC Oh yes, it completely changed everything. We had not been able to transplant children before that and, at about the same time, or very shortly after, we did Ben Hardwick, who survived for about a year or eighteen months and then died after a second transplant, we transplanted another little child of the same age called Andrew Hardwick and he's still alive and well, a real tough teenager working on his dad's farm now. So I think Esther Rantzen's programme was extremely valuable. It was a compassionate portrayal of the need for organ donation.

MB We're thinking of the eighties now and the progress you've made. It was a different world to the sixties, all those failed experiments. That must have been quite traumatic to face. Now we've got a working system where many people do well and the balancing of the books is very different. In the last few minutes of this particular interview, what I would like you to do is take me through from the eighties to now. What have been the real winning points, the real developments that we can put on the map, to condense the last ten years?

RC I think it's really to learn how best to use the drugs that we have, and select the patients and do the surgery and manage the medical side, as well as the anaesthetic and intensive care, so it's been more a honing down rather than a sudden leap upwards. We do have a whole lot of new drugs on the horizon to study and it's going to be very difficult because it's like compound mathematics really. You've got one agent and to learn to use that alone is not too difficult, When you've got two which may interact, it becomes more difficult, and three, which we have been working with

for the last fifteen or sixteen years, is difficult and we're only just beginning to get some sense out of it.

MB What is that combination of three, Roy?

RC Azathioprine, corticosteroids and cyclosporin. Now that there are other agents coming on – like FK506 and mycophenolate, and there's some very powerful antilymphocyte antibodies, both polyclonal and monoclonal, and it's going to take us a long time to sort out the best way of using them. I'm hoping that we're going to get towards a tolerance in man in which we would be able to use these powerful agents to manipulate the immune system at least temporarily to the same state that it's in, or a similar state, to what it's in during the embryo, so that we can produce tolerance or something akin to it. And we have some reasonable hopes that we may be able to do that. The liver effect that I've mentioned is a phenomenon that gives a lot of pointers as to how to go about it, and I did mention to you that the liver goes through a rejection and recovers, and that seems to be part of the development of tolerance. I envisage the mechanism as like a football match. You need to have an engagement that takes place and at the end of it shaking of hands and that's an acceptance of the graft. If you don't have the football match you won't get this, but the football match is likely to be deranged by hooligans, namely T-cells, useful in defence in time of war, but will spoil a football match, and so one needs to control those hooligans during the football match and afterwards perhaps. So that's where the drugs will come in. That would be my concept of the next stage in transplantation, the next major jump upwards. Then, because of the shortage of donors and all the ethical problems, the thing we're looking forward to is transplantation from animals to man. I don't think that's about to be solved. I think that's going to be a long haul. I don't think that's around the corner.

MB So, the jury is not in on that development?

RC Well, some people have mocked me greatly in this attitude, but I think we still have trouble stopping rejection in man to man, within a species, and it would be – I don't know whether arrogant is the right word or just simple-minded – to imagine that one can go from another species to man with more success. Since the closest to man are the primates and there's been no long-term success and we can't use chimpanzees because they are an endangered species, anything else is further away from man. A very convenient species would be the pig and there have been transgenic developments in the pig, putting human DNA to produce only one protein out of millions of proteins, but as every protein is different from the equivalent protein in pig, I think it's four hundred million years of separate Darwinian evolution. So, although this one transgenic protein may get over the first hurdle, I think there'll be others and not only immunological, but also metabolic biological hurdles, and circulation problems because the pig capillaries and the pig blood cells are not the same as in man.

MB So, it's a road with quite a lot of turnings still to travel?

RC I think so.

MB Roy, in the last few years, you've become a very senior figure in surgery, you've got national recognition and international recognition. Has that given you a real platform to do more for this field? Have you felt that you've rocked boats more effectively? I know you've stayed bolshy.

RC Well, I don't think it makes an awful lot of difference. I suppose people do listen to me a little bit more, but I think it's not so much that you want people to listen to you, but you want to do the experiments and show that there's no argument about it. That's what science is about, you say that something works, and it doesn't matter what opinions people have. If it works, they may not like it, they may not like you, they may not like the developments that will happen, but if it works, it works ...

MB Make them an offer they can't refuse.

RC Well, it's not even an offer, it's a fact.

MB Roy, let's come right to 1996, if I can, in the last moment or two. This family that you didn't see all that much of. Let's have an analysis of the family. You have six children?

RC Yes.

MB All living close to home still?

RC Yes, it's really nice because we had our fortieth wedding anniversary last year, and all the children and their children and their husbands and wives and girlfriends, there were eighteen of us in two houses in Spain, and we had a week's holiday, and I didn't hear one cross word. So, that was a great satisfaction.

MB My great point is that you see them on a regular basis now.

RC Yes, we see them at birthdays and Christmas and when there's a baby born and so on.

MB So, in a way, you're making up for all that time you didn't see them, I guess?

RC I suppose so, yes.

MB And we're going to talk about the painting and some of the leisure interests when we have more leisure, but there's a book out, on Monday?

RC On Monday, yes.

MB That's 16th December, and I'm looking forward to the launch of that. Talking about Art and Medicine.

RC 'Art, Surgery and Transplantation'. The main theme really is the

transplantation, trying to look at the human side of transplantation through images, mainly of patients and doctors, nurses and relatives.

MB Roy, for now until we meet in your studio and talk painting together, thank you.

RC It's a pleasure.