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HISTORICAL ANNOTATION

Witnessing medical history: an interview with Dr Rosemary Biggs

In February 1998, the Wellcome Trust's History of Twentieth Century Medicine Group held a Witness Seminar in London on 'Haemophilia: recent history of clinical management', organized by Professor Christine Lee and Dr Tilli Tansey. As a preliminary to the meeting, which will be published, Dr Rosemary Biggs was interviewed in her Oxfordshire home by Professor Lee and Dr Charles Rizza. This is a condensed version of that interview, edited by Tilli Tansey.

Prof. Lee: Why don't we begin with you telling us how you got into haemophilia?

Dr Biggs: I came to work in Oxford in about 1947 I think, and at that time the department was full of rather intelligent people who held the most extremely difficult intellectual conversations. I was totally bemused by this, and didn't understand a word that most of them said most of the time, but I settled down in the end to work for Professor Macfarlane. He first of all set us to determine the error of measuring things in the laboratory, like haemoglobin and red cell count, and so on, and then, inevitably, since he was interested, we also became interested in blood clotting. People became very fascinated with blood clotting, because it's such a wonderful trick isn't it? You tilt a tube and the contents fall out and then you do it again and it doesn't fall out. It's so sudden, and it's so easy to see. Whether it actually records anything or not is another matter, but it's certainly a very good endpoint and proved useful. I came to the conclusion in the end that usefulness was really the only thing. At a later stage I was studying the different kinds of coagulation defects that occurred in the Region, and of course haemophilia was the commonest. There was no question whatever of treating patients, and it wasn't really until the mid-fifties that Professor Douglas and I discovered a method of studying blood coagulation, which was called the 'thromboplastin generation test', which differentiated different kinds of defects. This name was used because it seemed that when the normal blood clotted there was a delay of about five minutes during which nothing happened and then quite suddenly a very strong coagulant was formed. We thought that something like tissue extract (thromboplastin) was formed in the blood. Then we found that classical haemophilia had a defect as measured by this test and we started studying different types and grades of haemophilia, and it occurred to Professor Macfarlane that if we could only measure factor VIII (the factor lacking in haemophilia) then we could make it and treat patients, and that was the task I undertook right through the 1960s. The thing was to correlate a level of factor VIII with how the patient reacted: could a patient have his tonsils out at this level, could he have his appendix out at that level, could he have a tooth out? The first patient we had was a chap with a gunshot wound who would certainly have died without treatment. So we treated him with some very early bovine factor VIII made by Dr Bidwell and he recovered. Then we tried to determine the most economic way of using this, now very valuable, factor VIII. If you could prevent bleeding with five per cent in the blood that was one thing, if you could cure it only with fifty per cent in the blood, that was another. Major surgery required very high levels of factor VIII; haemarthrosis, occurring only in very severely affected patients, required much less. So you could economize on the use of material. The other thing we had to study to get any sense of control was how long factor VIII stayed in the blood, and it turned out to have a very short half-life.

Once we had the clotting tests under control, the next problem turned up. This is how life is, isn't it? We couldn't get any factor VIII. It was greatly facilitated by Dr Judith Poole who discovered that factor VIII wasn't soluble in ice-cold plasma, it came out as a precipitate which you could separate and concentrate, so we had a very simple method of obtaining a concentrate by which we could attain higher levels of factor VIII in the blood. She had done the work in the early sixties. But I got to know her and visited her in San Francisco and she came to work with us for a year, in about 1975.

Dr Rizza: I remember the early days: the arguments that used to go on between you and Professor Macfarlane, about the value of pure research.

Dr Biggs: Oh yes, that was a very important discussion, because Professor Macfarlane wasn't scientifically interested in anything 'applied', it was just a useful by-product. What was important to him was exactly how the chemical interactions happened. My feeling was that if you waited until you knew that, before you considered treating patients, you would wait forever, because of course people still don't know how the blood clots do they? If it works, you take advantage of that fact. It is a totally different attitude to why you are doing the research. I think I started very much on the academic side, because I had come from being a botanist, working in Toronto for three years before I became a medical student.

Prof. Lee: Can you tell us how the patient organization began?

Dr Biggs: We assumed that no single general practitioner would see more than one haemophilic patient in their entire working life, if things turned out at random, and most would never see one. So the chances of them taking a sensible attitude to the condition was very, very remote and there was no way of teaching them, because there were thousands of general practitioners and we didn't know where the patients were. So first of all we developed Haemophilia Centres and this dated from when I decided to have a party at the Churchill Hospital. I invited all the people who might know anything about haemophilia. I figured that no one would resent a woman doing this, because it was only a party, and that's what women did – organize parties. The afternoon of the party was occupied by lectures, which of course they thought was perfectly appropriate and we then agreed to have a meeting every year. People liked that because you get to know people and you see a different place and so on. That was very successful, and from this group of people we developed the idea of Haemophilia Centres. The participants obviously wouldn't have come if they hadn't been interested and we developed a clientele all round the country, which consolidated the Haemophilia Centres. At this stage treatment was always carried out at the Centres [1].

Prof. Lee: Can you tell us some of the people at this time?

Dr Biggs: Well there was Professor Blackburn, from Sheffield.

Dr Rizza: He was the Chairman, wasn't he?

Dr Biggs: Yes. I was very determined not to be in the Chair, because, again, it was at that time slightly resented for a women to be in that position. I thought that since the main thing I want is for the work to get done, it was best for a nice man to be in the Chair. So Professor Blackburn did it for several years, and he was very competent.

Dr Rizza: There was Edgecumbe from Exeter.

Dr Biggs: Yes, that's right. You say the names, because my memory is absolutely gone now.

Dr Rizza: Professor Stuart Douglas from Glasgow, Professor Stewart from the Middlesex Hospital, London. Professor Roger Hardisty. Professor Ilsley Ingram from St Thomas' Hospital, London.

Prof. Lee: Was Katharine Dormandy around then?

Dr Biggs: She came a little bit later; she had an extremely good Haemophilia Centre at the Royal Free in London and she made a connection with the Haemophilia Society, because the next connection was to join up with the patients' association. After the first meeting I think the Haemophilia Society was always invited to send a representative to these meetings, as was the Ministry of Health.

Prof. Lee: As you gradually got your population of patients together, when did they start having regular follow-up at Oxford? Was it right from the beginning?

Dr Biggs: Well, they had permanent access to the Centre by telephone, or by visiting if they preferred, at any hour.

Prof. Lee: And when did you do the first surgery, using treatment?

Dr Biggs: That was the man with the gunshot wound. How he was working in such an unsuitable occupation I have no idea, but he let this gun off somehow or other and shot the whole of his side away, and had the most enormous gaping wound and was absolutely heading for disaster. But it was very interesting because after factor VIII treatment the tissue seemed to grow. You could watch it day by day, developing a layer of connective tissue and then some weeks later it was skin grafted and he made a complete recovery.

Prof. Lee: The other interesting thing I would like to hear from you is about haemophilia B and Mr Christmas. I was at a meeting about two weeks ago and there was a physician from Canada called Dr Jerry Teitle, who looked after Mr Christmas.

Dr Biggs: He arrived at our laboratory, and Dr John Poole, who was working there at the time, collected some blood from him; Dr Poole also had blood from another haemophilic patient and he mixed the two,

and the mixture clotted normally. So obviously they had different defects. This was one of the things that was detected by the thromboplastin generation test. The reagents for the test included alumina-treated plasma, serum and some form of phospholipid. If you left out any reagent, the test wouldn't work. So you really had three things you could measure. The defect in Mr Christmas was in the serum compartment, whereas the defect in the haemophilic was in the alumina–plasma department, so it was clearly different. It was very nearly Christmas 1952, and the *BMJ* agreed to take this paper at very, very short notice. We called it Christmas disease after the patient. And everybody read the article, because they thought it was something to do with overeating [2].

Dr Rizza: Some people thought it was a student's prank, that they had made the story up, and there were a lot of comments and complaints about the name.

Prof. Lee: When did you go to work at Oxford, Dr Rizza?

Dr Rizza: I went in 1958. Professor Stuart Douglas was with you then, wasn't he?

Dr Biggs: Yes, that's right. It was a very good time. There was an enormous amount of discussion. They were called haematological arguments, I remember, if nobody knew any of the facts. Because we discussed almost anything didn't we?

Dr Rizza: Well there were the teatime meetings of course. They were very good.

Dr Biggs: Yes, we had coffee in the middle of the morning, and there was always a big discussion over that. I don't know why, there was endless time wasn't there? And there were always far too many people. I think it was something to do with the aftermath of the war, when a lot of doctors who had been away for the war were given scholarships to study in various places and rather a lot of them seemed to come to Oxford. So the department was full of people who had no useful occupation, but were milling about doing various things.

Dr Rizza: Such as mixing blood from different patients! I always remember the coffee times. Juniors would come from various laboratories and sit down there and talk about almost anything. We drank coffee in the washing-up area, where we washed the glassware.

Dr Biggs: Yes, I remember that – the casualness of the way we treated things.

Dr Rizza: We used to have a Christmas party in the laboratory, having given the bench a wipe down before. There were plates of cakes and biscuits and sandwiches.

Dr Biggs: As far as I know nobody ever caught anything from it did they?

Dr Rizza: No. And mouth pipetting of course. Everyone mouth pipetted. Yellow plasma, clear plasma, it was all treated the same.

Dr Biggs: Oh yes. It never occurred to anybody that this stuff was infectious in any way.

Prof. Lee: What about the relationship with the transfusion centre?

Dr Biggs: That was tremendously important. The woman who ran the department at the time, Jean Grant, was extremely co-operative and she liked supplying plasma to Dr Bidwell. We had, you understand, absolutely nowhere to work, and this all took place in a hut in which factor VIII was made, tested and administered to the patients. There wasn't a place for giving anything to patients and the doctors lived in a caravan as far as I remember; those were the conditions under which we did all that work.

Prof. Lee: And you were using bovine factor VIII?

Dr Biggs: Yes, Professor Macfarlane calculated that if human blood from the transfusion practice was used, all the blood in the country had to be processed to get enough factor VIII. That didn't seem at all feasible, so he thought it would be better to start with animal blood, which was normally thrown away. Dr Bidwell used to go and collect blood at the slaughterhouse.

Prof. Lee: Presumably the animals had to be alive, for the blood to be caught?

Dr Biggs: Yes, it was all very nasty, the method of slaughtering was to cut their necks, and Dr Bidwell just used to catch the blood as it came out.

Prof. Lee: That's how they do the porcine preparation now.

Dr Biggs: None of it was very nice, and the patients turned out to be very resistant to this stuff; usually after the first course of treatment, they had reactions.

Prof. Lee: Why did people move to pigs?

Dr Biggs: If they were resistant to beef, it didn't necessarily mean they would be resistant to pig. It continued to be quite useful didn't it?

Dr Rizza: I think it had its place yes. I think Dr Bidwell also tried to make factor VIII from sheep didn't she?

Dr Biggs: Yes, she tried sheep. I can't remember what happened to the sheep.

Dr Rizza: The blood on the wool would coagulate very quickly.

Dr Biggs: Oh yes, that's right, it was very unsuitable. Poor animal, very unsuitable source of blood coming through all that coagulant material.

Dr Rizza: I think the slaughterhouse workers were not prepared to waste time shaving the neck.

Prof. Lee: When did you start getting into dentistry?

Dr Biggs: The main evidence determining whether the levels of factor VIII were adequate for surgery was done using observations following teeth extractions, because we believed that if we only took one tooth out we could stop the bleeding whatever happened. So the patients came and had one tooth out, and a course of treatment. I remember very plainly the first one, I don't know his name, but when he had had his tooth out he lay down to die, because he was sure the treatment was going to be no good, and after about an hour or two he sat up and couldn't imagine why he wasn't bleeding.

Prof. Lee: I have a patient who had all his teeth removed and he had one of these wire contraptions put on his mouth for three months to stop the bleeding afterwards, but he received bovine factor VIII.

Dr Biggs: After we found the first tooth extraction to be safe, we got more confident and we removed all teeth that would conceivably need to come out within the next five years. We thought that with subsequent reactions to the bovine factor VIII there was very little chance of them getting a second safe operation.

Prof. Lee: When I was a medical student at Oxford I have one memory of 1967, when we did orthopaedics, which was the ward of children, small boys. Tell us a bit about boys with haemophilia at that time.

Dr Biggs: They all went to the Nuffield Orthopaedic Centre which had developed a quite considerable expertise. They didn't have a lot of treatment. They had very slow careful manipulation of the joints to get them back into approximately a good position and the best result we ever hoped for was that they would fix in a position of reasonable usefulness for arms and legs. So they could raise your arm in a lesson, and stand on a useful leg. We weren't aiming at mobile joints, but simply trying to get them into a reasonably useful position. Of course it was at this time that the whole situation changed, because when we started treatment most of the patients didn't live to be grown up. The average age of death was 16, so there wasn't much purpose in giving education a top priority. Once the patients were going to live for a reasonable length of time they had to be educated, and well-educated, because they would never be able to do manual work. When they went to the Nuffield Orthopaedic Centre they used to get lessons and then the question arose: should further steps be taken in this direction? We co-operated with the Lord Mayor Treloar College at Alton, and they took haemophilic pupils [3].

Prof. Lee: When did they start taking boys with haemophilia?

Dr Rizza: About '64, '65 I think. They had 45 at one time: 45 boys with haemophilia.

Dr Biggs: Education was very profitable to them, because they were quite intelligent children. Perfectly able.

Prof. Lee: I have a number of adult patients now who were at Treloar and, sadly, they're also the ones who have died of AIDS, who knew each other when they were boys at the school.

Dr Biggs: The next thing that started to crop up was that patients started to get jaundice and we felt at the time that they were better alive and having jaundice than dead with haemophilia.

Prof. Lee: That is the most amazing comment. I get very irritated with patients now who are demanding compensation, because they have got hepatitis C from concentrate, but they wouldn't be alive to make those kinds of complaints if they hadn't been treated.

Dr Biggs: Yes, this is perfectly true. It's a very mixed thing. Of course, this is the age of people's rights. I don't think the patients seemed to have rights in my day, they were just grateful.

Prof. Lee: When did you start having directors reports, annual reports, annual returns from directors? Was that later?

Dr Biggs: No I think it was right from the beginning. I thought the important thing was to write the minutes of these meetings rather carefully so they came out very clearly directed. Of course there was a lot of what might have been called irrelevant discussion, so I always concentrated on what we

had decided to do. I tried to see that we did some of it during the year and then we could report on the results of that at the next meeting. That's how it came, from the beginning I think.

Dr Rizza: From the very first year, 1968–69. The other important thing was that when all those people got together for the first time, you realized that they all had the same problems with the administrators, such as not allowing money for staff or for premises; not so much for factor VIII because it wasn't being bought then, but they all had the same problems and that helped people to get together.

Dr Biggs: Yes, that's right. That really joined everyone together. The other thing, of course, one's colleagues may quarrel over scientific matters almost endlessly, but when it comes to treating patients, they all want to do the best they can. They could see that to be in this set-up really was of benefit both to the patients and to themselves. They could quote to their own administration what was expected of the Centre. In modern times the administrators are supposed to create things, but it's not my experience that they do make anything new. It isn't the job of administration is it? Administration runs a thing as it is, so it can't possibly innovate.

Prof. Lee: And what about carriers and giving people advice about having children? When did that become part of the whole practice

Dr Biggs: In part of the exploratory stage in the sixties we used to test the carriers and we found that statistically they had almost exactly half the amount of factor VIII of normals, but there was a big range. If a woman who might be a carrier had a low level of factor VIII she almost certainly was, but if she had a high level of factor VIII you couldn't be sure. So it became a partial diagnostic test. It was very difficult. People said to me you should stop them having children when they carry such a terrible disease, but the thing is that we were in no position to stop anybody having children, I mean the thing's ridiculous isn't it?

Prof. Lee: I suppose one of the things that must have changed things was the Abortion Act of 1967?

Dr Biggs: I can't remember. My feeling was that in talking to the patients some of them simply didn't want to be aborted. And you can't make people have an abortion can you? At least not in England! Besides which it was too reminiscent of the Nazi period wasn't it?

Prof. Lee: Yes and we forget how close you were to that period.

Dr Biggs: It was certainly very much in our minds and what I used to say to the patients and the parents of haemophilic children who felt guilty about it: 'everybody's got something, some people are terribly bad tempered, some people are very stupid, your son has haemophilia. I am sorry, but it's not very peculiar to have some trouble in life.'

Prof. Lee: Tell me about the patients. Did they move into Oxford when you were becoming such an important centre?

Dr Biggs: Yes, I believe it did happen. In Oxford we treated patients from the Isle of Wight to the middle of Wales. But as local centres developed, it was easier for patients to go for minor things to other centres, but Dr Rizza was always available for people to ring up and admit in an emergency, because by this time he had a ward [4].

Dr Rizza: In the early days there was no treatment, but when treatment came there was a need for beds and for people who could treat patients, and not people who looked down microscopes all the time.

Dr Biggs: What happened then, and this was a very big change actually, was that we borrowed beds from friendly physicians. They took responsibility for the patients because we weren't in a position to take responsibility, so we used to come in and treat them under the care of other physicians, such as Dr Mallam and Professor Witts. And of course the Nuffield Orthopaedic Centre's physicians. I think it was at this period that we started to agitate to get a physician on the department and Dr Rizza came to work with us. The whole thing had got totally out of hand because I wasn't a physician; I had never been trained as a physician.

Dr Rizza: That was 1966.

Dr Biggs: This was an enormous advance on anything we'd had before, because Dr Rizza was a real expert in treating patients and it was what he wanted to do. I remember he sat down in the chair in my office and I said 'what do you want to do with your life Charlie?' and he said 'I want to come and live in Oxford and treat haemophilic patients'.

Dr Rizza: Professor Macfarlane said quietly, 'you won't get involved in Oxford politics in this job'. And I said 'well thank you'.

Dr Biggs: The great anxiety among physicians was that the haemophilia specialist would snoop behind

the Radcliffe Outpatient Department and open a diabetic clinic. Why he should conceivably want to do that, nobody could explain to us, but they were very frightened of appointing a new physician to a department not under their control.

Prof. Lee: Why did you want to do haemophilia? Is that another story?

Dr Rizza: That's another story, which started back in Dundee. It's interesting how you can be affected by one person who shows you something interesting and you think that's what you want to do. I remember working with Dr Bill Walker, who became Professor of Medicine at Aberdeen. That's why I went to Oxford, because Dr Walker had been there, and I was interested in blood clotting as a houseman, and so when he said go there, and they accepted me, I stayed. That's how my interests started.

Dr Rizza: Another reason why Oxford was important I think was that since Dr Bidwell was making all that nice human factor VIII in Oxford and it wasn't available much elsewhere, people were sent to Oxford. We couldn't let it out, because it was so strictly controlled; we had to make sure that it was given under supervision, so that if anything went wrong we knew, and Dr Bidwell was particularly anxious that she should see what was happening with her material.

Dr Biggs: It was important wasn't it, because it was made under the most extremely unhygienic conditions to begin with and anything might have gone wrong. But, of course, she was very careful and it didn't go wrong.

Prof. Lee: What about home treatment? When did you start doing that?

Dr Biggs: I suppose that was towards the end of the sixties, was it?

Dr Rizza: Late sixties, early seventies. Yes.

Dr Biggs: It slowly dawned on us that no general practitioner was ever going to learn to treat the patients, and the parents of our haemophilics were extremely well informed as a rule – they obtained a certain amount of information from the Haemophilia Society – and they simply learned by experience. Then the obvious thing was to teach the parents how to do the venepunctures, and Dr Rizza had a clinic for that. The parents brought their children in and did the venepuncture under supervision.

Prof. Lee: Was there very much resistance from the medical or the administrative hierarchy, because it was a very unusual thing to do?

Dr Rizza: It was very unusual. We had more difficulty getting the nurses to be allowed to do venepunctures than getting the parents to do it. It seems strange that here was a qualified woman who the Royal College of Nursing said shouldn't do this, but you could teach a lay person to do it in their own home.

Prof. Lee: When did you first have domiciliary nurses; was that the same period?

Dr Rizza: About 1978–79. It gradually came because we were doing more and more home therapy and we felt an obligation to make sure that the home circumstances were reasonably hygienic and that the parents were coping. It was one thing to see them doing well in the clinic, but it was nice to go round and see that the dog wasn't on the table at the same time as they were giving the factor VIII, which happened sometimes.

Prof. Lee: When this move to home therapy was going on how did we compare with Europe? Were we ahead, behind, or was everybody the same?

Dr Rizza: I think the UK was a bit ahead of Europe, but a little bit behind America, because the Americans had brought in the first large amounts of factor VIII from the companies and that came about in 1971–72. That's really what set things going, the large volumes of factor VIII coming from the companies, and the Americans had this earlier.

Dr Biggs: Then we found the tremendous importance of having good blood in the preparations. The American preparations were particularly liable to cause jaundice because the blood was collected from down-and-outs hanging about wherever the blood transfusion service depots were. In America they all got a fee for giving blood; they subsisted by donating blood.

Dr Rizza: They also had very, very large pools of blood, whereas in the UK to begin with the pools were quite small.

Prof. Lee: What do you mean by quite small?

Dr Rizza: We had 500 to their 10 000 donations. On one occasion commercial factor VIII was held up at Heathrow and the patients couldn't get it because the government wouldn't pay for it. Dr Biggs, Professor Blackburn and, I think, Professor Ingram and Dr Jones wrote saying that it was unforgivable to see all this factor VIII at Heathrow Airport locked in a warehouse, while patients were bleeding around the country, and the government not prepared to pay for it.

Dr Biggs: Yes, that's right. That's when money raised it's ugly head wasn't it? Our own hospital was very good about the money wasn't it?

Dr Rizza: Factor VIII was supplied by the pharmacy.

Dr Biggs: We used more than half the area's money for medicines, just on the haemophilic patients.

Dr Rizza: This was about 1971, 1972. You had a very close association with the chief pharmacist, Mr Trillwood.

Dr Biggs: Yes, he was a very nice man, really interested, and determined that we should never be short of material.

Dr Rizza: It started with the porcine material. He made sure that we had plenty of porcine factor VIII and plenty of bovine when it went commercial. To begin with Dr Bidwell made the material and then it went to various companies like Crookes and Maws. They took it into large-scale production when Dr Savage from Maws came and was instructed on making factor VIII, and then he developed his own method. He also developed his own method of assay.

Dr Biggs: Oh yes, a really individual person. People are entitled to their own views, their own ways of doing things. It can be very important to people to have their own method. Judith Poole had her own assay method, and two factions developed in America as to who used my method and who used her method. They were, in fact, almost identical.

Prof. Lee: What was Professor Macfarlane doing at the time. Was he in his laboratory, or did he get involved with the patients?

Dr Biggs: He didn't really get involved except with some of the first patients from St Bartholomew's Hospital. One was a set of triplets with haemophilia. He was deeply involved with the early treatments using bovine factor VIII.

Prof. Lee: I know the triplets. One of them has just had a coronary artery stenosis and had a stent inserted, which is quite extraordinary. We thought we would find some underlying thrombotic tendency in him, but we haven't. He's now 67, has just retired and, apart from this recent problem, he has had a very good life.

Dr Biggs: They were a wonderful set because there were the triplets, and another brother with haemophilia.

Prof. Lee: The older brother has a level of 5%, and 10 years ago had carcinoma of the oesophagus resected. Last summer he developed acute cholecystitis, and our transplant surgeon at the Royal Free removed his gall bladder. Nowadays we cover surgery with continuous infusion. We have to use high-purity factor VIII, either the monoclonal product or recombinant, but there was a supply problem with monoclonal product at the time and he had the surgery using recombinant.

Dr Biggs: They were a wonderful family. They used to come and occupy our entire library with the big table in the middle and sit round and have a big family discussion with me.

Prof. Lee: My patient talks quite often of their childhood and says his mother was the most amazing person who would make sure she got the best for them. It must have been quite extraordinary to have triplets with haemophilia.

Dr Biggs: They weren't inactive as children, they were absolutely all over the place. Professor Macfarlane had them in Barts when they were three and four and said they were menaces about the laboratory.

Dr Rizza: We are back to you and Professor Macfarlane again. He was the pure scientist and you were the practical scientist.

Dr Biggs: Yes, he was a very pure scientist. He liked the electron microscopic surfaces of platelets, that really gave him pleasure. Yes, different sorts of minds.

Prof. Lee: When did Professor Duthie come on the scene, when he took over from Professor Trueta?

Dr Rizza: 1966. Professor Trueta retired in '66.

Dr Biggs: He went back to Spain didn't he? He came over here on account of the Spanish civil war, because he was a Republican and he would have been killed in Spain at that time.

Dr Rizza: He made his name in the Spanish civil war by showing that when soldiers or civilians had severely damaged limbs, the best thing they could do was put them in Plaster of Paris and leave them. Don't do anything else, don't try to nail them together, just immobilize them in Plaster of Paris, and let them get better, and they did.

Dr Biggs: Yes, it was an extraordinary phenomenon. They just simply got better.

Prof. Lee: When was the first big real elective orthopaedic surgery done, as opposed to emergency

surgery? I suppose we are talking about joint replacements or arthrodesis.

Dr Biggs: I think the seventies.

Dr Rizza: There was a patient with factor IX deficiency, who gave all the blood to enable you to do the factor IX assay, and his grandson is now working in molecular genetics, unravelling the factor IX defect. So our patient gave his blood in those days and now his grandson is doing important scientific work.

Dr Biggs: He's still alive?

Dr Rizza: No he died at the age of 77. He was very nice. He regularly gave blood to make the substrate. Some patient's blood was not very good as a substrate, but his was very good.

Dr Biggs: It was an art as well as a science. Some people's blood just wouldn't do well.

Prof. Lee: And were you involved with the child whose arm was amputated?

Dr Rizza: It was Dr Bill Walker who sent him down with his parents, this poor little boy with this gangrenous arm just hanging there.

Dr Biggs: I remember taking a first look at that child and thinking 'oh no!'. He was such a lovely little boy wasn't he?

Dr Rizza: He was a charming child. I went to Scotland last year on holiday and met him; he's about 40 now. He's a very nice man, an architect. He only has one arm, but he challenged me to a game of golf. I remember at the time that Dr Donald Handley was a Registrar, and he was superb at venepuncture. The child was frantic with worry until Dr Handley treated him and after that he wasn't nearly so bad. He had to be anaesthetized several times to have venepunctures done [5].

Prof. Lee: The other thing that we forget is the needles that you had. Now we have all the butterfly needles, all the disposables.

Dr Rizza: That to me was probably one of the most important advances, the disposable needle and syringe. I remember as a houseman sharpening needles, poking a wire through to make sure they were clear, because there was nothing more irritating than having a child, getting the needle in a vein after some difficulty and then finding it stuck, and the blood won't come back. The needle was so firmly attached to the syringe you can't get the syringe off to try another.

Dr Biggs: Nobody in a position of authority would do anything about it. They never did venepunctures; they didn't see any difficulties, somebody else did them and the fact that the apparatus was totally abysmal didn't worry them at all. When you are involved with the interaction of clotting factors, the fact that someone can't get a needle into a vein is beneath notice.

Prof. Lee: It's actually not so long ago, because I did my house jobs in 1969–70, and when we put a drip up, we had two metal needles in a drip pack and if you used them up, they had to be resterilized.

Dr Rizza: Well, I saw plastic needles, disposable needles and syringes, in 1962, because we had them in the laboratory and it was a godsend; because the needle was so sharp and the syringe's barrel moved, they didn't stick.

Prof. Lee: I think we had plastic needles for venepuncture then, but not for drips. That must have really made a major difference to the treatment of those patients.

Dr Rizza: That was a huge difference, and another thing that people forget is the plastic bag. Without the plastic bag there wouldn't be any cryoprecipitate. That's why Dr Judith Poole got on so quickly because she was working in a closed system; she didn't have to extract the plasma with the risk of contamination. They do this in a plastic bag by just squeezing it over. Those were two huge advances. And the children noticed it. They knew when the needle was blunt; they would tell you the needle was blunt. But you had to get on with it. The older haemophiliacs can't understand the fuss that the younger haemophiliacs make. They can't understand why they have so much trouble with pain relief. They managed perfectly well without any, because the concentrates are so good and ease the pain. As soon as you start giving a concentrate the pain starts to diminish within five minutes. The older men can't understand why younger men need so much pethidine and morphine and palfium. But as you were saying earlier older men realize that there may have been several occasions when they would have died without factor VIII, whereas the younger people accept their relative normality.

Dr Biggs: Yes, I can quite see that that could happen now. 'Oh I am not having another dose now.' Things like that. I think they must play that game mustn't they, but they must learn gradually.

Dr Rizza: Well, it's a different perception isn't it. You remember the ... boys, sadly, now both dead.

I met old Mrs ... and she tells very graphically the story of going from Woodstock to the Radcliffe Infirmary with a bleeding boy under each arm, all the way in the bus, apologizing to the other passengers that blood was dripping all down the corridor. She would walk to see you and Professor Macfarlane with a child in each arm, one with a cut head and one with a bleeding tooth. And that was her life. The number of times she got on the bus. She didn't call an ambulance. She didn't have a car.

Dr Biggs: I remember her. She was a very good supporter of the Haemophilia Society.

Prof. Lee: It's been a fascinating afternoon, thank you very much for sharing these memories with us.

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